JOURNAL OF GENERAL CHEMISTRY OF THE USSR

Volume 28, Number 4 April 1958

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XIII. SYNTHESIS OF N,N-DIETHYLAMIDES AND N-ARYLAMIDES OF ACIDS WITH THE AID OF SILICOANHYDRIDES OF SATURATED MONOBASIC ORGANIC ACIDS

Iu. K. Iur'ev and Z. V. Beliakova

N-Substituted amides of organic acids are usually prepared by the reaction of alkyl amines and anhydrides or acid chlorides of the appropriate acids, whereby only 50% of the alkyl amine can be utilized for the production of the N-alkyl- or N,N-dialkylamide of the acid, since the remaining 50% is consumed in the formation of a second reaction product— the salt of the amine. Thus, when diethyl amine is reacted with acetic anhydride, N,N-diethylacetamide [1] and diethylamine acetate are obtained. When diethyl amine reacts with acetyl chloride, propionyl chloride, and butyryl chloride, the corresponding N,N-diethylamides of acetic [2], propionic [3], and butyric [2, 4] acids and diethylamine hydrochloride are obtained.

The N,N-diethylamides of the acids are also prepared directly from the acids and diethylamine by heating to 230°. In this way the N,N-diethylamides of acetic [5] and isovaleric [6] acids have been prepared. A series of aliphatic N,N-dimethylamides [7] has been prepared with yields of 70-80% by heating a mixture of the acid and dimethylamine to 200° in an autoclave.

The last method, however, does not always permit attaining good yields, and for this reason recourse is had more frequently to the preparation of the N,N-diethylamides from the acid chlorides.

N-Arylamides, as is well known, can be prepared directly from the acid and aniline; however, not infrequently the anhydrides [8, 9] and acid chlorides [10, 11] of the acids are also used for the preparation of the anilides.

In the present work we used tetraacyloxysilanes— mixed anhydrides of orthosilicic and organic acids— for the preparation of N,N-diethylamides and N-arylamides. These had been used successfully in place of the anhydrides and acid chlorides of the acids by K. D. Petrov [12] for the acylation of aromatic compounds (benzene and toluene) and by us for the acylation of heterocyclic compounds— thiophene [13], selenophene [14], pyrrole and indole [15], and also for the synthesis of aromatic α,β-unsaturated acids [16].

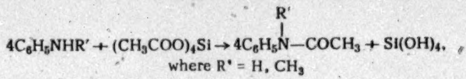
It should be noted that it is indicated in the literature by Friedel and Ladenburg that acetamide is formed by the reaction of ammonia with the silicoanhydride of acetic acid [17].

Having shown previously that tetraacyloxysilanes enter into all the reactions that are characteristic of acid anhydrides, although less actively [18], we reacted the silicoanhydrides of acetic, propionic, n-butyric, n-valeric, isovaleric, and n-caproic acids with diethylamine and obtained good yields (60-90%) of the corresponding N,N-diethylamides of acetic, propionic, n-butyric, n-valeric, isovaleric, and n-caproic acids:

$$(RCOO)_4Si + 4NH(C_2H_5)_2 \rightarrow 4RCON(C_2H_5)_2 + Si(OH)_4$$

$$(R{=}CH_3,\ C_2H_5,\ C_3H_7,\ n\text{-}C_4H_9,\ iso\text{-}C_4H_9,\ C_5H_{11})$$

When aniline was reacted with tetraacetoxysilane, acetanilide was obtained in 90% yield.



$$4C_6H_5NHR' + (CH_3COO)_4Si \rightarrow 4C_6H_5\overset{\overset{R'}{|}}{N}-COCH_3 + Si(OH)_4,$$

where $R' = H, CH_3$

The method proposed by us for the preparation of amides and arylamides of acids by the reaction of amines with tetraacyloxysilanes is convenient because, first, tetraacyloxysilanes are very easily prepared from silicon tetrachloride and the appropriate acids in benzene and do not require any purification before use, and second, because in this reaction all the amine should go into the formation of the corresponding substituted amide.

EXPERIMENTAL

Methods of Preparing N,N-Diethylamides

In a 250-ml three-necked flask, fitted with a stirrer, a reflux condenser with a calcium chloride tube, and a gas delivery tube reaching to the bottom of the flask, was placed 100 ml of anhydrous benzene, 0.15 g-mole of organic, saturated, monobasic acid, and 0.045 g mole of silicon tetrachloride, and the mixture was heated on a water bath first at 60-70° and then to boiling, until the evolution of hydrogen chloride completely ceased. To completely remove the hydrogen chloride from the mixture, a stream of dry air was passed through it for 15-20 minutes. The mixture was cooled with ice water, the gas delivery tube was replaced by a dropping funnel, and 0.1 g-mole of diethylamine was added drop by drop. The reaction mixture thereupon heated up and often a precipitate of silicic acid separated out immediately. When all the amine had been introduced, stirring of the mixture was continued for 1 hour at room temperature and then it was heated for 4-5 hours on a water bath, first at 40-50° and afterward to boiling. The mixture was cooled and the precipitate of silicic acid was filtered off and washed with benzene. The combined benzene solution was washed with 2 N sodium hydroxide solution, dried with anhydrous sodium sulfate and, after the benzene was distilled off, the residue was distilled in vacuo. The yield of N,N-diethylamide obtained was calculated on the basis of the diethylamine used in the reaction.

N,N-Diethylacetamide. Using an acetic acid: diethylamine ratio of 1.5:1, we obtained from 9 g of acetic acid, 5.2 ml of silicon tetrachloride, and 7.3 g of diethylamine 9.6 g (83.5%) of N,N-diethylacetamide; b. p. 88-89° (26 mm).

With an acetic acid: diethylamine ratio of 1:1, we obtained from 9 g of acetic acid, 5.2 ml of silicon tetrachloride, and 10.95 g of diethylamine 10.45 g (60.5%) of N,N-diethylacetamide; b. p. 93-94° (35 mm).

With an acetic acid: diethylamine ratio of 2:1, we obtained from 12 g of acetic acid, 7 ml of silicon tetrachloride, and 7.3 g of diethylamine 10.4 g (90%) of N,N-diethylacetamide; b. p. 93-94° (35 mm).

The N,N-diethylacetamide thus obtained had the following constants: b. p. 93-94° (35 mm), n_D^{20} 1.4401, d_4^{20} 0.9048, MR_D 33.55; calc. 33.53.*

Found %: N 12.22, 12.35. $C_6H_{13}ON$. Calculated %: N 12.16.

Literature data: b. p. 184-184.8° (747 mm); n_D^{20} 1.4396; d_4^{20} 0.9045 [19].

N,N-Diethylpropionamide. From 11.1 g (0.15 g-mole) of propionic acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 11.5 g (89%) of N,N-diethylpropionamide: b. p. 77° (12 mm), n_D^{20} 1.4419, d_4^{20} 0.8972, MR_D 38.12; calc. 38.15.

Found %: N 11.14, 11.21. $C_7H_{15}ON$. Calculated %: N 10.84.

Literature data: b. p. 191° [3].

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*In the calculation of the additive values of MR_D for N,N-diethylacetamide and the N,N-diethylamides of the other acids obtained in our work, the atomic refraction of nitrogen was taken as 2.508, the value established by B. V. Ioffe for tertiary amides (except formamides) [19].

N,N-Diethylbutyramide. From 13.3 g (0.15 g-mole) of n-butyric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 12.85 g (90%) of N,N-diethylbutyramide:

b. p. 79-80° (8 mm), n_D^{20} 1.4431, d_4^{20} 0.8884, MR_D 42.75; calc. 42.76.

Found %: N 9.96, 10.01. $C_8H_{17}ON$. Calculated %: N 9.78.

Literature data: b. p. 206°, 106° (24 mm), 92° (12 mm) [4].

N,N-Diethylvaleramide. From 15.3 g (0.15 g-mole) of n-valeric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 7.3 g (0.1 g-mole) of diethylamine we obtained 12.45 g (79%) of N,N-diethylvaleramide:

b. p. 94-95° (10 mm), n_D^{20} 1.4452, d_4^{20} 0.8808, MR_D 47.53; calc. 47.38.

Found %: N 9.18, 9.29. $C_9H_{19}ON$. Calculated %: N 8.91.

N,N-Diethylvaleramide is not described in the literature.

N,N-Diethylisovaleramide. From 15.3 g (0.15 g-mole) of isovaleric acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 10.95 g (0.15 g-mole) of diethylamine we obtained 16.15 g (70%) of N,N-diethylisovaleramide:

b. p. 77-78° (5 mm), n_D^{20} 1.4422, d_4^{20} 0.8764, MR_D 47.5; calc. 47.38.

Found %: N 9.06, 9.11. $C_9H_{19}ON$. Calculated %: N 8.91.

Literature data: b. p. 93-95° (14 mm) [21].

N,N-Diethylcaproamide. From 17.4 g (0.15 g-mole) of n-caproic acid, 5.2 ml (0.045 g-mole) of silicon tetrachloride, and 10.95 g (0.15 g-mole) of diethylamine we obtained 14.55 g (61%) of N,N-diethylcaproamide:

b. p. 95-96° (5 mm), n_D^{20} 1.4467, d_4^{20} 0.8784, MR_D 52.07; calc. 52.00.

Found %: N 8.48, 8.41. $C_{10}H_{21}ON$. Calculated %: N 8.18.

N,N-Diethylcaproamide is not described in the literature.

Acetanilide. To a cooled benzene solution of silicoacetic anhydride prepared as described above from 12 g (0.2 g-mole) of acetic acid and 7 ml (0.06 g-mole) of silicon tetrachloride, there was added with continuous stirring, drop by drop, 9.3 g (0.1 g-mole) of aniline in 30 ml of anhydrous benzene. The reaction mixture was heated on a boiling water bath for 10 hours, and the precipitate of silicic acid that had separated was filtered off and washed with hot benzene. The crystals of acetanilide that precipitated when the benzene solution was cooled were filtered off. When the benzene had been distilled off from the mother liquor, more crystals of acetanilide were obtained, which were recrystallized from water. Yield 12.2 g (90%); m. p. 115°.

A mixed melting point test with known acetanilide showed no depression.

Literature data: m. p. 115° [22].

N-Methylacetanilide. The synthesis was carried out as described for acetanilide. The precipitate of silicic acid was filtered off, washed with hot benzene, and when the benzene had been distilled off from the combined filtrates, the remaining crystals were pressed out on a porous plate. From 12 g (0.2 g-mole) of acetic acid, 7 ml (0.06 g-mole) of silicon tetrachloride, and 10.7 g (0.1 g-mole) of N-methylaniline we obtained 13.4 g (90%) of N-methylacetanilide with m. p. 102° (from alcohol). A mixed melting point with known N-methylacetanilide showed no depression.

Literature data: m. p. 101-102° [10].

SUMMARY

Reaction of silicoanhydrides of saturated, monobasic, organic acids with secondary aliphatic amines may serve as a convenient method for the synthesis of N,N-dialkylamides of the acids. By this method the N,N-diethylamides of acetic, propionic, n-butyric, n-valeric, isovaleric, and caproic acids were prepared in good yields (60-90%).

The possibility of preparing N-arylamides in this way was demonstrated by the examples of the acylation of aniline and methylaniline with silicoacetic anhydride.

In the synthesis of N-substituted amides of acids, the use of tetraacyloxysilanes has the advantage over the use of the acid chlorides or the anhydrides of the acids.

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Received December 26, 1956

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*Original Russian pagination. See C. B. Translation.

CATALYTIC CONVERSIONS OF HETEROCYCLIC COMPOUNDS

LIII. CONVERSION OF HOMOLOGS OF OXAZOLE TO HOMOLOGS OF THIAZOLE

Iu. K. Iur'ev and I. G. Zhukova

In spite of the existence of a deep-seated difference in the chemical nature of compounds of the furan series and the oxazole series, which is manifested, for example, in the almost complete absence of acidophobic properties in the oxazoles and clearly expressed acidophobic properties in the furans, the oxazoles also display a number of characteristics that are typical of the furans and are explained by the structural similarity of these heterocyclic systems.

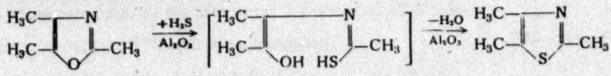
Thus, the replacement of a cyclically bound oxygen atom by an imino group characteristic of the furans — the conversion of furan and its homologs by the action of ammonia or amines to pyrrole [1] and N-substituted pyrroles — finds a complete analogy in the very easy formation of imidazoles from oxazoles. Compounds of the oxazole series are converted into imidazoles by heating with alcoholic [2] or aqueous ammonia solution [3] or by heating with formamide [4]; the reaction of oxazoles with aniline [2] also proceeds very readily and results in the formation of N-phenylimidazoles.

The reaction of oxazoles with hydrogen sulfide, which should lead to the formation of the corresponding thiazoles, has not been investigated; the conversion, recently described in the literature, of 2-methyl-4-isopropylideneoxazolone-5 to 2,5,5-trimethylthiazoline-4-carboxylic acid by the action of hydrogen sulfide [5] cannot serve as an example of the conversion of the parent oxazole ring to the thiazole ring, since it is the result of a more complex change in the molecule.

But the reaction of oxazole and its homologs with hydrogen sulfide presents considerable interest with respect to the characteristics of the oxazole ring: the formation of thiazoles from oxazoles in this reaction would be a complete confirmation of the chemical similarity of these structurally close cyclic systems with their cyclically bound oxygen atom.

A study carried out by us of the catalytic conversion of methyl homologs of oxazole by the action of hydrogen sulfide showed that the alkyloxazoles, like other five- and six-membered oxygen-containing heterocyclic compounds, both of aromatic nature and saturated, undergo this general reaction of replacement of cyclically bound oxygen by sulfur. As a result of the action of hydrogen sulfide in the presence of aluminum oxide on 2,4-, 2,5-, and 4,5-dimethyloxazole, and also 2,4,5-trimethyloxazole, they are converted respectively to 2,4-, 2,5-, and 4,5-dimethylthiazole and 2,4,5-trimethylthiazole. As also in the case of the conversion of furan to thiophene, the conversion of the oxazole ring proceeds, no doubt, through the intermediate stage of formation of the 1,4-mercaptohydroxy compound, by the dehydration of which the thiazole ring originates.

It should be noted that the yield of the methyl homologs of thiazole was small and amounted in all to 10-15%, while it was possible to isolate from the products of catalysis only up to 20% of unchanged alkyloxazole, and the catalyst was covered with a thick incrustation of carbonaceous deposit — products of deep-seated decomposition of the alkyloxazole molecule.



The presence of unchanged alkyloxazole in the products of catalytic conversion by the action of hydrogen sulfide is evidence, on the one hand, of the stability of the oxazole ring to the action of a reagent of acid character and, on the other hand, of the comparatively slight stability of this ring on contact with aluminum oxide heated to 300-375°. A suggestion concerning the possible reversibility of the reaction – oxazole + $H_2S \rightleftarrows$ thiazole + H_2O – was not confirmed: in the catalyzate obtained by passing a mixture of 4,5-dimethylthiazole and steam over aluminum oxide at 375° 4,5-dimethyloxazole was not found.

Comparison of the results obtained by the synthesis described in the literature of imidazoles from substituted oxazoles with the results obtained by us in the catalytic conversion of oxazoles to thiazoles shows that replacement of the cyclically bound oxygen atom in oxazole homologs by the imino group or sulfur depends in great degree on the chemical nature of the reagent under the influence of which this exchange takes place (ammonia, alkylamines, arylamines, hydrogen sulfide). However, in contrast to what has been observed in similar conversions of furan and its homologs [6], it appears that in the oxazole series the replacement of bridge oxygen by other heteroatoms proceeds with greater completeness the lower the acidity of the reagent employed.

On this rule depends the possibility of obtaining the imidazoles in high yields (up to 70%) [3], the N-arylimidazoles in lesser yields (up to 50%) [2], and the thiazoles in small yields from the oxazoles.

We were not able to accomplish the catalytic conversion of 2-methylbenzoxazole to 2-methylbenzothiazole: 50% of unchanged 2-methylbenzoxazole was recovered from the reaction, while the remaining portion of it underwent decomposition. In this connection it should be noted that Theilig [4] did not obtain 2-methylbenzimidazole by the action of formamide on 2-methylbenzoxazole, while the alkyloxazoles upon reaction with this reagent gave good yields of the corresponding alkylimidazoles.

Inasmuch as the catalytic conversion studied by us of the isomeric dimethyloxazoles, and also the trimethyloxazole, to the respective thiazoles proceeded with almost identical yields, it is apparent that because of the presence of a tertiary nitrogen atom in the ring this reaction has little dependence on the position and number of the methyl groups or on the temperature within the range 300-375°.

As is well known, in the furan series the position of the methyl groups in the ring and their number have a substantial effect on the yield of the corresponding thiophenes.

EXPERIMENTAL

Alkyloxazoles and their constants. 2,5-Dimethyloxazole was obtained in the amount of 30 g by the method of Treibs [7]:

b. p. 115-117° (760 mm), n_D^{21} 1.4394, d_4^{21} 0.9856, MR_D 25.97. $C_5H_7ON\vDash_2$. Calculated: 27.74; EM_D – 1.79. Literature data [8]: b. p. 116-117°, n_D^{25} 1.4365; [9]: n_{He}^{20} 1.439, d_4^{20} 0.997, EM_D – 1.72.

4,5-Dimethyloxazole was obtained in the amount of 100 g by the method of Bredereck and Theilig (II):

b. p. 115-117° (755 mm), n_D^{20} 1.4432, d_4^{20} 0.9966, MR_D 25.82. $C_5H_7ON\vDash_2$. Calculated: 27.74; EM_D – EM_D – 1.92.

Found %: N 14.28. C_5H_7ON. Calculated %: N 14.42.

In the work of Bredereck and Theilig [11] an incorrect boiling point (129-135° at 760 mm) for 4,5-dimethyloxazole was mistakenly given without indicating the other constants.

4,5-Dimethyloxazole methiodide. 0.9 g of 4,5-dimethyloxazole and 1.4 g of methyl iodide were heated for 1 hour at 100°: m. p. 137° (from anhydrous alcohol with precipitation by ether).

Found %: N 5.86, 5.80. $C_6H_{10}ONI$. Calculated %: N 5.85.

2,4-Dimethyloxazole was prepared by the method of Theilig [4] in the amount of 40 g:

b. p. 106-108° (750 mm), n_D^{20} 1.4389, d_4^{20} 0.9757, MR_D 26.18. $C_5H_7ON\vDash_2$. Calculated: 27.86; EM_D – 1.56.

Methiodide: m. p. 247°.

Literature data [4]: b. p. 103-110° (760 mm); [12]: b. p. 97-107°. Methiodide: decomp. temp. 235°; [9]: b. p. 95°, n_{He}^{20} 1.414, d_4^{20} 0.931; EM_D − 1.24.

2,4,5-Trimethyloxazole was prepared by the method of Bredereck and Theilig [11] in the amount of 30 g:

B. p. 137-138° (760 mm), n_D^{20} 1.4425, d_4^{20} 0.9569, MR_D 30.76. $C_6H_9ONF_2$. Calculated: 32.36; EM_D −1.60. Picrate: m. p. 113° (from anhydrous alcohol). Adduct with $HgCl_2$: m. p. 166° (from anhydrous alcohol).

Literature data [13]: b. p. 132-133°, n_D^{25} 1.4412, d_{25}^{25} 0.9566; [7]: b. p. 135° (720 mm). Adduct with $HgCl_2$: m. p. 165°; [10]: Picrate with m. p. 115°.

Conversion of alkyloxazoles to alkylthiazoles. 2,5-Dimethylthiazole. Nine g of 2,5-dimethyloxazole was passed over aluminum oxide at 350° at the rate of 0.3 ml/min. in a current of hydrogen sulfide. The catalyzates obtained in three experiments were saturated with potassium carbonate and extracted with ether. After the ether was distilled off from the ether extract, which had been dried with anhydrous potassium carbonate, the residue was fractionated, yielding 3.6 g (13% of the amount introduced into the reaction) of unchanged 2,5-dimethyloxazole (b. p. 115-117°, n_D^{20} 1.4390) and 3.6 g of 2,5-dimethylthiazole, which had the following constants:

b. p. 151-153° (760 mm), n_D^{20} 1.4898, d_4^{20} 1.0280, MR_D 32.76. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.73.

Yield 13% of theoretical, calculated on the basis of the 2,5-dimethyloxazole used.

Found %: N 12.17. C_5H_7NS. Calculated %: N 12.39.

Picrate: m. p. 172° (from anhydrous alcohol).

Literature data [14]: b. p. 148.9°-150.9° (743 mm), 153° (758 mm); [9]: b. p. 153° n_{He}^{20} 1.511, d_4^{20} 1.058.

At 300° the yield of 2,5-dimethylthiazole (calculated on the basis of the 2,5-dimethyloxazole) was 13%, at 375°−12%.

4,5-Dimethylthiazole. From three experiments using 8.9 g of 4,5-dimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.4 ml/min. in a current of hydrogen sulfide, there was obtained, after appropriate treatment of the reaction product, by distilling off 2.7 g (10%) of unchanged 4.5-dimethyloxazole (b. p. 115-117°), and by fractionating in vacuo, 4.5 g of 4,5-dimethylthiazole that had the following constants:

b. p. 75-77° (47 mm), n_D^{20} 1.5193, d_4^{20} 1.0699. MR_D 32.12. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.37.

Yield 15.5% of theoretical calculated on the basis of the 4,5-dimethyloxazole used.

Picrate: m. p. 187° (from anhydrous alcohol).

Found %: N 16.21, 16.36. $C_{11}H_{10}O_7N_4S$. Calculated %: N 16.36.

Literature data [15]: b. p. 75° (47 mm).

2,4-Dimethylthiazole. From three experiments using 6.9 g of 2,4-dimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.5 ml/min. in a current of hydrogen sulfide, there was obtained, after appropriate treatment of the catalyzate, by distillation of the reaction product, 2.4 g (12%) of unchanged 2,4-dimethyloxazole (b. p. 106-108°, n_D^{20} 1.4390) and 2.4 g of 2,4-dimethylthiazole that had the following constants:

b. p. 67-68° (50 mm), n_D^{20} 1.5095, d_4^{20} 1.0513, MR_D 32.17. $C_5H_7NSF_2$. Calculated: 33.49; EM_D − 1.32.

Yield 12.0% calculated on the basis of the 2,4-dimethyloxazole used.

Picrate: m. p. 137-138° (from anhydrous alcohol).

Found %: N 16.72, 16.74. $C_{11}H_{10}O_7N_4S$. Calculated %: N 16.36.

Literature data [16]: b. p. 142.5-143°, d^{15} 1.0601, picrate with m. p. 137-138°; [15]: b. p. 70-71° (50 mm); [9]: b. p. 143°, n^{20}_{He} 1.509, d^{20}_4 1.057; [18]: picrate with m. p. 135°.

2,4,5-Trimethylthiazole. From three experiments using 6.9 g of 2,4,5-trimethyloxazole each, which was passed over aluminum oxide at 375° at a rate of 0.5 ml/min. in a current of hydrogen sulfide, there was obtained, after the usual treatment of the reaction product and distillation, 3.2 g (12%) of unchanged 2,4,5-trimethyloxazole (b. p. 137-139°) and 2.4 g of 2,4,5-trimethylthiazole that had the following constants:

b. p. 64-66° (20 mm), n^{20}_D 1.5023, d^{20}_4 1.0327, MR_D 36.37. $C_6H_9NSF_2$. Calculated: 38.11; EM_D – 1.74.

Yield 10% of theoretical calculated on the basis of the 2,4,5-trimethyloxazole used.

Found %: N 11.37, 11.32. C_6H_9NS. Calculated %: N 11.00.

Picrate: m. p. 132° (from anhydrous alcohol).

Literature data [17]: b. p. 165-166° (717.5 mm), d^{16} 1.0130, picrate with m. p. 133°; [15]: b. p. 65-67° (20 mm).

SUMMARY

The isomeric dimethyloxazoles (2,4-, 2,5-, and 4,5-) and 2,4,5-trimethyloxazole, when acted upon by hydrogen sulfide in contact with aluminum oxide at an elevated temperature undergo, like other five- and six-membered oxygen-containing heterocycles, replacement of bridge oxygen by sulfur with the formation of the corresponding dimethylthiazoles (2,4-, 2,5-, and 4,5-,) and 2,4,5-trimethylthiazole.

Because of the presence of a tertiary nitrogen atom in the oxazole ring the yield of the isomeric dimethylthiazoles prepared catalytically by the conversion of the corresponding oxazoles has little dependence on the position of the methyl groups in the ring of the latter.

Catalytic conversion of the oxazole ring to the thiazole ring proceeds according to the same reaction mechanism as that established for the analogous conversion of furan to thiophene, but the oxazole ring shows considerably greater stability than that of furan toward the action of an reagent of acid character— hydrogen sulfide— under these conditions.

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Received December 14, 1956

RADICAL AND ION ALKYLATION OF THE AROMATIC RING

VI. REACTIONS OF DIPHENYLCHLOROMETHANE WITH TOLUENE AND BENZENE

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Little work has been devoted to the use of diphenylchloromethane in alkylation reactions. Boeseken [1] studied this reaction with benzene in the presence of $AlCl_3$ and showed that the normal product, triphenylmethane, was formed in insignificant yield and the chief products were diphenylmethane (35%) and triphenylchloromethane (30%). Pfeiffer [2] pointed out the formation of triphenylmethane in the reaction of diphenylbromomethane with benzene in the presence of $SnCl_4$. Thermal (and catalytic with $ZnCl_2$) alkylation of phenols with diphenylchloromethane was accomplished by Alphen [3], and with diphenylbromomethane by Busch [4]. On heating diphenylbromomethane and pyridine in sealed tubes Chichibabin [5] isolated a negligible amount of benzohydrylpyridine along with tetraphenylethylene (50%) and diphenylmethane (20%).

Continuing an investigation of the use of a copper catalyst for alkylation [6, 7] we undertook a study of reactions with diphenylchloromethane. In a previous article [6] it was reported that thermal and catalytic benzylation of a number of aromatic compounds was accomplished, and on the basis of the data obtained it was assumed that the reaction proceeds with homolytic redistribution of the bonds in the reaction complex without the formation of free radicals.

The choice of diphenylchloromethane as the object of the present work was explained, on the one hand, by the insufficient investigation of alkylation reactions with benzohydryl halides, and on the other hand, by the striving to obtain complete information on the mechanism of these reactions. There was an indication [8] that diphenylchloromethane on treatment with metallic silver forms free radicals: in the absence of air tetraphenylethane was formed in quantitative yield; in oxygen the principle products were various oxygen-containing compounds along with a small amount of tetraphenylethane (2-8%). Under the reaction conditions studied we also might expect the appearance of free radicals under the influence of the copper on the diphenylchloromethane and in connection with this a change in the course of the synthesis of benzohydryl-substituted aromatic compounds.

We have shown that the reaction of diphenylchloromethane with toluene in the presence of small amounts of copper (0.1 g-equiv.) at 115-140° proceeds with the formation of p-benzohydryltoluene (54%) as the main product; the o-isomer and tetraphenylethane are formed as negligible contaminants. In some reactions diphenylmethane also was found. Carrying out the reaction in a current of nitrogen or of oxygen did not change the course of the process.

We were not able to accomplish the introduction of the benzohydryl group into the benzene molecule under analogous conditions. Triphenylmethane was obtained in negligible yield at 200°. Heating equimolecular amounts of copper and diphenylchloromethane in benzene solution yielded tetraphenylethane (67.5%); triphenylmethane was formed in very trifling amount in some reactions. Carrying out the reaction in oxygen gave the same results. It was established that CuCl and HCl, as in the benzylation reactions also, are not catalysts.

The data presented show that the transition from benzyl chloride to diphenylchloromethane does not result in a change in the reaction mechanism: neither in the alkylation nor in the dimerization reaction (synthesis of tetraphenylethane in benzene solution) do free radicals appear. Otherwise the formation of oxygen-containing products must be expected on carrying out the reaction in oxygen [8]. This conclusion also is confirmed by the thermal reactions with diphenylchloromethane, which proceed differently than thermal benzylation reactions. It is known that distillation of diphenylchloromethane at atmospheric pressure is accompanied by decomposition. Engler [9] obtained tetraphenylethylene and HCl in this way. Anschütz [10], when he reproduced these experiments, noted the formation of tetraphenylethane and HCl (the products were not fully investigated).

We have shown that thermal decomposition of diphenylchloromethane at 300-305° leads to the formation of tetraphenylethylene (89%) and HCl. In benzene also tetraphenylethylene (92%) and HCl are formed. In toluene and cyclohexane the yield of tetraphenylethylene decreases (47 and 56% respectively); besides this, a nearly equivalent amount of diphenylmethane is formed (40 and 38.5%). The decomposition reaction in toluene, which is not deep-seated, yields tetraphenylethylene and tetraphenylethane. To explain the formation of these products it may be assumed that in the first stage the dissociation of diphenylchloromethane to a diphenylmethyl radical and an atom of chlorine (I) occurs. The diphenylmethyl radical then may undergo dimerization (II) and disproportionation (III):

$$(C_6H_5)_2CHCl \rightarrow (C_6H_5)_2CH\cdot + Cl. \qquad (I)$$

$$2(C_6H_5)_2CH\cdot \rightarrow (C_6H_5)_2CHCH(C_6H_5)_2 \qquad (II)$$

$$4(C_6H_5)_2CH\cdot \rightarrow 2(C_6H_5)_2CH_2 + (C_6H_5)_2CH{=}CH(C_6H_5)_2 \qquad (III)$$

At 300° the disproportionation (III) dominates. In the absence of a solvent (and in benzene) the chlorine atom dehydrogenates the diphenylmethane to the diphenylmethyl radical, which then undergoes a similar conversion, so that the final product is tetraphenylethylene. In solvents that have more active hydrogens the solvent undergoes dehydrogenation (the C—H bond in diphenylmethane is weaker, but the solvent is present in great excess).

The fact that tetraphenylethylene is not formed through a stage of tetraphenylethane was shown by experiments on the decomposition of diphenylchloromethane in it. The reaction proceeded with much tar formation, and diphenylmethane was isolated (42%) with only a trifling admixture of tetraphenylethylene.

The decomposition of diphenylchloromethane in the presence of diphenylmethane led, as might be expected on the basis of the assumed mechanism, to the formation of tetraphenylethylene (86.4%) while the amount of diphenylmethane remained unchanged.

In other cases products of the conversion of radicals through the solvent have not been discovered up to the present time. The possibility of decomposition of diphenylchloromethane with the formation of a diphenylmethylene biradical also should be taken into account.

Summing up what has been stated above, we arrive at the conclusion that the mechanism of the catalytic reactions described in the presence of copper is similar to the mechanism of benzylation: the reactions proceed with homolytic redistribution of the bonds within the reaction complex, in the formation of which the catalyst takes part. In thermal reactions of diphenylchloromethane, in contrast to such reactions of benzyl chloride, free radicals play a part.

EXPERIMENTAL

Reactions of diphenylchloromethane with toluene were carried out in a flask with a reflux condenser connected through a calcium chloride tube with an absorbing bottle. The diphenylchloromethane and then the toluene were added to the copper, and the mixture was heated on a sand bath for 3-7 hours at 112-140° (thermometer in the liquid) until the evolution of HCl almost completely ceased. At the end of the reaction the mixture was filtered off from the inorganic residue and the latter was treated several times with hot toluene. The toluene used for washing was combined with the filtrate which, after the solvent was distilled off, was fractionated in vacuo. The p-benzohydryltoluene fraction was always obtained as an oil, which crystallized only upon prolonged standing. But addition to the oil of a small amount of methyl or ethyl alcohol or ether caused rapid crystallization as a result of transition to a solution of the o-isomer. The melting point of the p-isomer was 70-71° (literature data: 69-70° [11]). From methyl alcohol (which was usually used) the o-isomer separated on long standing, m. p. 80-82° (literature data 80-83° [12]).

The tetraphenylethane was pressed out on a porous plate and recrystallized from benzene. M. p. 208-210°. A mixed melting point test with a known sample gave no depression. Diphenylmethane, which was obtained in several reactions, was demonstrated by the preparation of the 4,4'-dinitro derivative with m. p. 181-185° [13] (Table 1).

TABLE 1

Reactions of Diphenylchloromethane with Toluene

Molecular ratio $(C_6H_5)_2CHCl : Cu : C_7H_8$	Reaction conditions			Yield of reaction products (%)	
	temperature	time (hours)	medium	p-benzohydryltoluene	tetraphenylethane
1 : 0.1 : 3	96°	12	Air	9.6	—
1 : 0.1 : 10	111—113	7.5	Nitrogen	16.9	5.9
1 : 0.1 : 3	115—138	7.5	Air	54	5.9
1 : 1 : 3	112—140	2.5	Nitrogen	41.5	30.8
1 : 0.09 : 2.7	118—197	5	Nitrogen	38.4	2.8
1 : 0.1 : 3	112—140	7	Oxygen	44.5	3.5

Reactions of diphenylchloromethane with benzene at 84-120° were carried out similarly to the experiments with toluene. The method of workup of the mixture, when large amounts of tetraphenylethane were formed, was different: after the reaction was completed, a 5-10 times excess of benzene was added and the hot mixture was filtered off from the inorganic residue. Most of the solvent was removed by distillation, and from the small residue the tetraphenylethane crystallized. M. p. 207-208°. The mother liquor was distilled in vacuo.

Triphenylmethane usually was mixed with tetraphenylethane and decomposition products. It was separated from tetraphenylethane by washing 2-3 times with alcohol. The crystals obtained upon evaporation of the alcohol were purified by recrystallization from benzene. M. p. 91-93°; a mixed sample with a known preparation melted at 91-93° (Table 2).

TABLE 2

Reactions of Diphenylchloromethane with Benzene

Molecular ratio $(C_6H_5)_2CHCl : Cu : C_6H_6$	Reaction conditions		Reaction products (%)	
	temperature	time (hours)	tetraphenylethane	triphenylmethane
1 : 0.1 : 3	87—92°	13	2.8	—
1 : 0.1 : 3*	150	7.5	2.8	—
1 : 0.12 : 3*	200	7.5	3	4
1 : 1 : 5.2	85—86	7.5	51	2.4
1 : 1 : 2	86—120	3	64	—
1 : 1 : 5.2**	84—100	6	67.5	2.4
1 : 1 : 5***	85— 86	7	55	—

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*Experiments were carried out in an autoclave.

**Benzene was introduced in two portions with an interval of 1.5 hours.

***Experiment in a current of oxygen.

TABLE 3

Decomposition of Diphenylchloromethane by Heating to 300-305° in the Course of 7-7.5 Hours

Amount of diphenyl-chloro-methane (g)	Solvent and amount (g)	Yields of reaction products				
		tetraphenylethylene		diphenylmethane		tar
		g	(%)	g	(%)	
5.1		3.7	89	—	—	0.5
5.1	Benzene (6.2)	3.85	92.3	—	—	0.3
5.1	Toluene (6.2)	1.95	46.8	1.7	40	1
5.1	Cyclohexane (6.35)	2.35	56.5	1.6	38.5	0.2
5.1	Tetraphenylethane (3)	0.05	1.2	1.8	42.5	2.45
2.55	Diphenylmethane (1)	1.8		1		0.2

Thermal decomposition of diphenylchloromethane. The reactions were carried out in sealed ampoules, which were heated in an autoclave to 300-305° in the course of 7-7.5 hours. When low-boiling solvents were used, the appropriate solvent was poured into the autoclave. Before closing the ampoule in some instances (decomposition in diphenylmethane) thorough cooling was required (solid carbon dioxide). The contents of the ampoule were carefully extracted with a suitable solvent or benzene. The crystals that separated from the cooled solution were removed and the mother liquor was fractionated (Table 3).

SUMMARY

1. Reactions of diphenylchloromethane with toluene and benzene in the presence of copper have been studied. With toluene (0.1 g-equiv. of copper) p-benzohydryltoluene was obtained (54%); with benzene (equimolecular amount of copper) the main product was tetraphenylethane (68%).

New experimental data are adduced which confirm the opinion expressed previously that free radicals are not formed under the conditions considered.

2. Thermal decomposition reactions of diphenylchloromethane have been studied in a number of aromatic compounds and in cyclohexane; a free-radical mechanism has been proved for them.

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Received January 2, 1957

CHLORINATION OF FIVE- AND SIX-MEMBERED CYCLANES*

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The investigation of chlorination processes of the cycloparaffins has repeatedly attracted the attention of many investigators who have sought to find ways of going from the chemically inert cycloparaffins to the reactive halogen derivatives.

The halogenation reactions of cyclanes and alkanes are in many respects similar to each other, but they also have some differences.

The literature on the chlorination of cyclanes contains a limited amount of experimental data. Many studies on the halogenation of five- and six-membered cyclic hydrocarbons have been carried out with petroleum fractions; the conditions of halogenation are not fully enough indicated.

To the early studies in this field belong the classic investigations of V. V. Markovnikov [1], who prepared monochlorocyclohexane with b. p. 142° (750 mm) by the action on cyclohexane of moist chlorine in the cold and with irradiation by sunlight. When dry chlorine was used, Markovnikov heated the hydrocarbon almost to its boiling point. This process led to the formation also of polychloro derivatives. By distillation of the chlorination products of cyclohexane Markovnikov separated two isomeric dichlorocyclohexanes.

A careful investigation was carried out by E. Fortey [2], who conducted a photochemically catalyzed chlorination of cyclohexane. The hydrocarbon was placed together with a small amount of iron filings in an apparatus equipped with a reflux condenser, and a current of dry chlorine was passed through it in the direct sunlight at room temperature for several hours. A mixture of di- and polychloroderivatives was obtained on fractional distillation of the chlorination products; the monochloro derivative was not formed. Fortey also carried out the chlorination of cyclohexane with dry chlorine in the cold with irradiation by daylight for 3 hours. In this case he isolated monochlorocyclohexane and two isomeric dichlorocyclohexanes by fractional distillation of the reaction product.

N. D. Zelinskii [3] carried out the vapor-phase chlorination of cyclohexane in a specially constructed apparatus which met the following conditions: "1) The monochloride was immediately taken out of the sphere of the reaction, 2) only the low-boiling fractions of the mixture were continuously admitted to the sphere of reaction, 3) the chlorine introduced into the reaction was in excess of the hydrocarbon vapors." By chlorination in the light for 27.5 hours N. D. Zelinskii obtained a product with a yield, calculated as monochloride, of 90%. By photochemical chlorination of cyclohexane in a Zelinskii chlorinator, N. I. Shuikin [4] obtained chlorocyclohexane in 38.4% yield calculated on the starting hydrocarbon; the yield based on reacted cyclohexane was 83.4%.

A more complete study of the halogenation reactions of the simplest cyclopentane and cyclohexane hydrocarbons might not only be of considerable interest, but also reveal a way for the utilization of these hydrocarbons, for example, for the preparation of cyclic secondary alcohols and other derivatives. Recently the halogen derivatives of the cyclanes have found wide use in agriculture as insecticides.

EXPERIMENTAL

The starting cyclanes had the following properties: cyclopentane—b. p. 49-49.5° (755 mm), d_4^{20} 0.7455, n_D^{20} 1.4063; cyclohexane—b. p. 80.5-81° (752 mm), d_4^{20} 0.7788, n_D^{20} 1.4263.

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*L. N. Karchenko participated in conducting the experiments.

The constants found were close to the data in the literature [5].

For convenience in comparing the results obtained by chlorination by different methods, a single procedure was adopted in the present work for working up the chlorination products: they were carefully washed with sodium carbonate and with water, were dried with calcium chloride, and then subjected to fractional distillation in vacuo on a column with an efficiency of 40 theoretical plates. On the basis of the data on the boiling limits of the individual fractions and other of their physicochemical properties the content of mono-, di- and polychlorides was determined in the chlorination products. As characteristics of the chloro products their constants and their chlorine content were determined.

TABLE 1

Physicochemical Properties of Individual Chloro Derivatives

Chlorocyclane fractions	Boiling temperatures (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Chlorine content (%)	
				found	calc.	found	calc.
Monochlorocyclopentane fraction	114—115 (752)	1.0050 - 1.0052	1.4500 - 1.4512	27.81 - 28.3	27.96	33.0, 33.5	33.3
Dichlorocyclopentane fraction	79.5—81.0 (50)	1.1758 - 1.1792	1.4682 - 1.4686	32.76 - 32.86	32.82	50.25, 50.35	50.31
Monochlorocyclohexane fraction	140—142 (752)	0.9990 - 0.9993	1.4623 - 1.4625	32.44 - 32.55	32.58	29.00, 29.15	29.08
Dichlorocyclohexane fraction	105.5—115.0 (50)	1.1670 - 1.1704	1.4811 - 1.4814	37.02 - 37.22	37.44	46.30, 46.43	46.37

On the basis of the first rough experiments on the separation of the chlorination products of cyclopentane and cyclohexane it was recognized as expeditious, for convenience in carrying out serial analyses, to take fractions for the monochlorocyclanes, dichlorocyclanes, and polychlorocyclanes having the properties given in Table 1, corresponding to the literature data [2].

The first group of experiments (1-22) — the thermal chlorination of cyclopentane and cyclohexane — was carried out in a catalytic tube filled with inert material (glass beads), heated by an electric furnace with an automatic regulator. Experiments were set up with moist and dry chlorine. In this way the optimum temperature and ratio of hydrocarbon to chlorine were shown. The results of the experiments are given in Table 2.

From the data given in Table 2 it follows that a change in the temperature of chlorination within the limits from 250 to 270° (with other conditions constant) does not have an appreciable effect on the yield of monochlorocyclopentane. The presence of traces of moisture in the reaction field has a substantial effect on the character of the chlorination of cyclopentane. In case of the use of dry chlorine the yield of polychlorides is somewhat increased and the formation of monochloropentane is decreased. In experiments with moist chlorine, however, the yield of the monochloride is increased, with a decrease in the formation of polychlorides.

A study of the chlorination of cyclohexane showed (Table 3) that the optimum temperature for this process under the conditions used was 320-340°. Here also the presence of moisture in the reaction field had substantial significance. The use of moist chlorine led to an increase in the yield of monochloride and a decrease in the formation of polychlorides.

The second group of experiments (54-71) was devoted to a study of the photochemical chlorination of cyclanes in the vapor phase in the apparatus of N. D. Zelenskii [3] in daylight. The initial temperature of the reaction mixture in the upper globe of the chlorinator was 30-35°; the temperature of the experiment was further maintained within the limits 40-45°. The results of the experiments are given in Tables 4 and 5, from

TABLE 2

Thermal Chlorination of Cyclopentane. Duration of Experiments 180 Minutes, 17.5 g Cyclopentane and 7.6 l Chlorine Used (molar ratio cyclopentane : chlorine = 1 : 1.4)

Expt. No.	Temperature	Yield of condensate (g)	Composition of condensate (%)			
			unreacted cyclopentane	monochloride	dichlorides	polychlorides
			Dry chlorine			
5	250°	22.5	10.8	36.9	34.3	18.0
10	260	22.4	3.8	37.8	39.5	18.9
14	270	22.4	—	39.3	41.7	19.0
			Moist chlorine			
16	250	22.6	10.2	41.4	35.0	13.4
19	260	22.5	2.7	43.0	38.0	15.3
22	270	22.5	—	45.3	39.0	15.7

TABLE 3

Thermal Chlorination of Cyclohexane. Duration of Experiments 180 Minutes; in Each Experiment 14 g of Cyclohexane and 5.0 l of Chlorine were Used

Expt. No.	Temperature	Yield of condensate (g)	Composition of condensate (%)			
			unreacted cyclohexane	monochloride	dichlorides	polychlorides
			Dry chlorine			
23	280°	19.4	27.7	36.3	36.0	—
27	290	19.4	26.8	37.5	35.7	—
31	300	19.4	21.3	39.0	37.3	2.4
35	320	19.4	12.5	39.7	38.5	9.3
39	330	19.4	3.7	41.3	42.5	12.5
42	340	19.4	—	41.9	43.8	14.3
			Moist chlorine			
45	320	19.5	11.5	43.9	39.0	5.6
49	330	19.4	3.3	46.0	40.3	10.4
53	340	19.4	—	48.3	41.0	10.7

the data of which it is seen that, as in the case of thermal chlorination also, the best yield of monochlorides was obtained when moist chlorine was used. But carrying out the reaction with dry chlorine, markedly increased the content of more highly chlorinated cyclanes in the reaction products.

The third group of experiments (72-99) — photochemical chlorination of cyclanes in the liquid phase — was carried out by our using chlorine admitted to the reaction in the apparatus shown schematically in the figure.

The hydrocarbon was placed in the cylindrical reactor (1), illuminated at a distance of 18 cm by an electric lamp (2) with a power of 200 w. Chlorine from the cylinder (3) passed through the Tishchenko bottle (4) with concentrated sulfuric acid and was introduced through the rheometer (5) into the hydrocarbon at room temperature (15-17°) through the capillary tubules (6) which were lowered to the bottom of the reactor. The gaseous reaction products escaped from the reactor into the condenser (7). The hydrocarbon vapors were condensed to a liquid, which ran back into the reactor.

TABLE 4

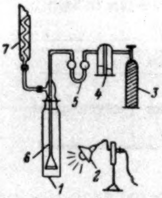
Photochemical Chlorination of Cyclopentane in the Vapor Phase. Duration of Experiments 4.5 Hours; in Each Experiment 35 g of Cyclopentane and 11 l of Chlorine were Used (molar ratio 1 : 1)

Expt. No.	Yield of condensate (g)	Composition of condensate (%)			
		unreacted cyclopentane	monochloride	dichlorides	polychlorides
		Dry chlorine			
54	40.3	10.4	34.5	35.3	22.8
57	40.5	10.7	32.7	34.9	21.7
		Moist chlorine			
59	40.4	10.0	39.7	32.5	17.0
61	40.6	10.6	40.0	32.1	16.6

The hydrogen chloride passed through the condenser into a absorbing apparatus, where it was collected in water.

Because of a shortage of cyclopentane its chlorination was not fully investigated, but even those few experiments that were carried out with it showed that with a molar ratio of cyclopentane and chlorine of 1 : 1.5 and an experiment time of 5.5 hours the condensate contained 60.4% monochlorocyclopentane, 24.5% dichlorides, and 15% polychlorides. The results of the experiments with cyclohexane are given in Table 6.

From the data of this Table it is evident that with an increase in the ratio of cyclohexane to chlorine from 1 : 1 to 1 : 6.5 the formation of polychlorides was notably increased and the formation of monochlorides decreased.



Scheme of apparatus for the photochemical chlorinization of hydrocarbon. (Explanation in text).

TABLE 5

Photochemical Chlorination of Cyclohexane in the Vapor Phase. Duration of Experiments 4.5 Hours; in Each Experiment 42 g of Cyclohexane and 10.9 l of Chlorine (molar ratio 1 : 1) were used

Expt. No.	Yield of condensate (g)	Composition of condensate (%)			
		unreacted cyclohexane	monochloride	dichlorides	polychlorides
		Dry chlorine			
63	47.0	10.6	33.8	35.6	20.0
65	47.3	10.4	31.0	35.3	20.3
		Moist chlorine			
68	46.9	10.4	40.7	31.9	17.0
71	47.2	10.3	41.0	32.3	16.4

TABLE 6

Photochemical Chlorination of Cyclohexane in the Liquid Phase

Expt. No.	Duration of experiments (hrs)	Used		Moles cyclohexane : chlorine	Yield of condensate (g)	Composition of condensate (%)			
		cyclohexane (g)	chlorine (liters)			monochloride	dichlorides	trichlorides	polychlorides
				Dry chlorine					
85	19.0	14.0	12.3	1:3.5	26.0	16.0	23.0	21.5	39.2
89	16.0	14.0	16.2	1:4.5	26.6	—	29.3	23.3	47.3
93	19.4	14.0	23.4	1:6.5	33.7	—	9.8	20.9	69.2
				Moist chlorine					
97	13.0	14.0	12.2	1:3.5	26.0	20.2	23.0	26.3	30.5
99	19.4	14.0	23.4	1:6.5	34.0	—	19.0	30.7	50.3

As also in the other methods of chlorination, here the use of moist chlorine led to some increase in the yield of monochlorides.

SUMMARY

1. The thermal and photochemical chlorination with dry and moist chlorine of cyclopentane and cyclohexane in the liquid and vapor phases has been studied.

2. The conditions have been found that permit obtaining, as desired, principally mono- or polychlorinated products.

3. The advantages of liquid-phase chlorination of five- and six-membered cyclanes have been demonstrated.

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Received January 7, 1957

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*In Russian.

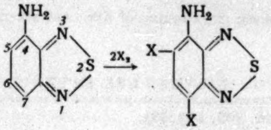
STUDIES IN THE FIELD OF THE CHEMISTRY OF 2,1,3-THIODIAZOLE

VI. CHLORINATION AND BROMINATION OF 4- AND 5-AMINOBENZO-2,1,3-THIODIAZOLES

V. G. Pesin and A. M. Khaletskii

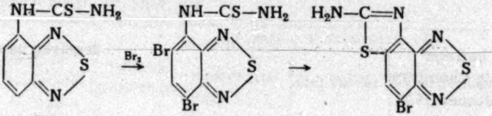
We have shown previously [1] that 4- and 5-aminobenzo-2,1,3-thiodiazoles are easily acylated under the usual conditions for aromatic amines. In the present communication data are presented on an investigation of chlorination and bromination reactions of 4- and 5-aminobenzo-2,1,3-thiodiazoles.

The high reactivity characteristic of aniline is fully observed in 4-aminobenzo-2,1,3-thiodiazole (I). Thus, upon chlorination and bromination of the latter the main products are the 4-amino-5,7-dihalobenzo-2,1,3-thiodiazoles (II). When equimolecular amounts of the reactants are used for the reaction, part of the 4-aminobenzo-2,1,3-thiodiazole does not enter into the reaction, and the corresponding disubstituted compounds are formed in approximately 40-45% yield. When the conduct of the reaction is based on an estimation of the production of dihalogen derivatives (where X is chlorine or bromine), the latter are formed in high yields.



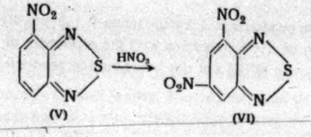
(I) (II)

A high reactivity also is noted for acylated 4-aminobenzo-2,1,3-thiodiazole. Thus, for example, when benzo-2,1,3-thiodiazole-4-thiourea (III) is brominated, mainly the dibromo derivative is formed, which is converted to the corresponding derivative of benzothiodiazole (IV).

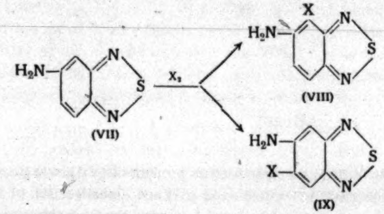


(III) (IV)

These data show that the direction of substitution in the hydrocarbon ring is determined by the amino group, since no effect at all of the thiodiazole ring appears. The same fact is noted in the literature [2] for nitration of 4-nitrobenzo-2,1,3-thiodiazole (V); the second nitro group enters position 6, i.e., substitution occurs under the influence of the nitro group already present (VI) (the effect of the thiodiazole ring does not make itself felt).

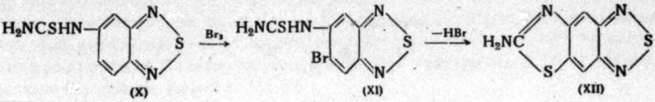


Thus, on chlorination and bromination of 4-aminobenzo-2,1,3-thiodiazole (VII) the latter behaves like a typical aromatic primary amine. This predominant effect of substituent in the hydrocarbon ring on the place of entrance of another substituent is observed in still greater degree in the chlorination or bromination of 5-aminobenzo-2,1,3-thiodiazole. In this case the halogen can enter the 4- and 6-positions of the 5-aminobenzo-2,1,3-thiodiazole (VIII) and (IX).



It has been shown previously [1-5] that on nitration and sulfonation the nitro and sulfo group, respectively, enter the 4-position of the aromatic ring, i.e., the thiodiazole ring directs the substituent in these reactions into the 4-position. On the basis of what has been stated it might be assumed that on chlorination or bromination of 5-aminobenzo-2,1,3-thiodiazole the chlorine or bromine would enter the position most favored by the joint orientation of the amino group and the thiodiazole ring, i.e., position 4. But actually, as we have shown, bromine (and probably chlorine) in this reaction replaces the hydrogen in the hydrocarbon ring in position 6.

Similarly in the bromination of benzo-2,1,3-thiodiazole-5-thiourea (X) the bromine also replaces the hydrogen on C_6; the bromine derivative formed (XI) is converted into the corresponding derivative of benzothiazole (XII).

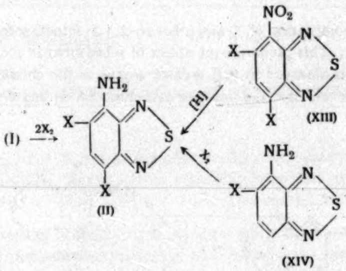


Since we have recently shown [4, 6] that benzo-2,1,3-thiodiazole, and also 1',2'-naphtho-2,3-thiodiazole [6] enter into an addition reaction with chlorine or bromine, it was of interest to investigate the halogenation (chlorination, bromination) of 4-aminobenzo-2,1,3-thiodiazole under conditions similar to those for the halogenation of the 2,1,3-thiodiazole derivatives mentioned.

For this purpose 4-aminobenzo-2,1,3-thiodiazole (I) was subjected to both chlorination and bromination in the fused state. The products isolated were 4-aminobenzo-5,7-dichloro- and 4-amino-5,7-dibromo-2,1,3-thiodiazole, respectively. Thus, when 4-aminobenzo-2,1,3-thiodiazole (fused) is reacted with chlorine or bromine a substitution reaction occurs, and not an addition, as is observed on reaction of benzo-2,1,3-thiodiazole (fused) with chlorine (or bromine).

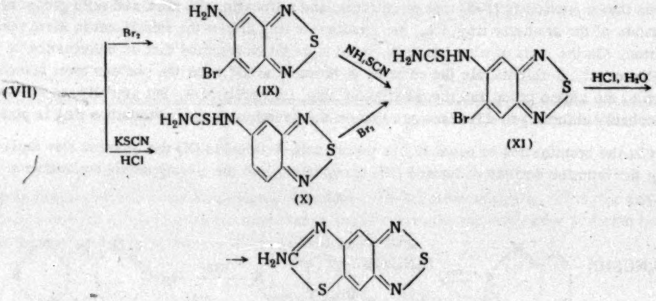
These and some other data show that the aromatic character of benzo-2,1,3-thiodiazole is intensified in its derivatives, for example in amino-, nitro-, and some halobenzo-2,1,3-thiodiazoles, while on the contrary the unsaturated character is weakened.

The structure of the halogenation products of 4-aminobenzo-2,1,3-thiodiazole, i.e., the position of the halogen, was proved by comparison of their properties with the properties of the reduction products of 5,7-dihalo-4-nitrobenzo-2,1,3-thiodiazole (XIII) and the halogenation products of 5-halo-4-aminobenzo-2,1,3-thiodiazole (XIV) [7].



X – halogen

The position of the bromine in (IX), the bromination product of (VII), was proved by conversion of the latter into 5,6-(2'-aminothiazole)benzo2,1,3-thiodiazole (XI) and identification of this derivative with the same compound obtained by the bromination of benzo-2,1,3-thiodiazole-5-thiourea (X).



Furthermore, this same compound (XI) was prepared by us from the thiocyanation product of 5-aminobenzo-2,1,3-thiodiazole, and also by the condensation of 2,5,6-triaminobenzothiazole with thionylaniline.

The chlorination of 4- and 5-aminobenzo-2,1,3-thiodiazoles was carried out with dichloramine in the presence of concentrated hydrochloric acid in acetic medium, and the bromination was conducted in acetic acid medium.

The derivatives of thiourea were synthesized by the reaction of the hydrochlorides of the appropriate amines with potassium thiocyanate or ammonium thiocyanate in chlorobenzene [8-12] or in water [13-17]. Cyclization of the thiourea derivatives was carried out by bromination of the latter in chloroform at 0° [13, 18]. As regards the starting 4- and 5-aminobenzo-2,1,3-thiodiazoles, they were synthesized in 85-87% yield by a reaction previously developed by us [19].

EXPERIMENTAL

4-Amino-5,7-dichlorobenzo-2,1,3-thiodiazole. a) Chlorination with dichloramine in acetic acid solution. To 1 g of 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, in 7 ml of 98% acetic acid and 1.65 g of dichloramine at 12° was added with continuous stirring over a period of 15 minutes a solution of 2 ml of concentrated hydrochloric acid in 7 ml of acetic acid. After 1 hour's stirring the precipitate that had separated was filtered off and washed in succession with a small amount of acetic acid and water. 1.15 g of a yellow crystalline material (80%) was obtained. After recrystallization from alcohol the crystals melted at 172.5-173° and gave no depression in a mixed melting point test with the reduction product of 4-nitro-5,7-dichlorobenzo-2,1,3-thiodiazole.

b) Chlorination in the fused state with gaseous chlorine. Chlorine was passed into a fusion of 4-aminobenzo-2,1,3-thiodiazole (0.5 g) to saturation; after the reaction mass was cooled, 0.7 g of a dark brown material was obtained, which after recrystallization from 50% alcohol (in the presence of carbon) melted at 171-173°. A mixed melting point test with known 4-amino-5,7-dichlorobenzo-2,1,3-thiodiazole showed no depression.

4-Amino-5,7-dibromobenzo-2,1,3-thiodiazole. a) Bromination in acetic acid solution. To 0.5 g of 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, in 10 ml of acetic acid was added from a dropping funnel with constant stirring a solution of 0.4 ml of bromine in 11 ml of acetic acid. After 1 hour's stirring the precipitate that had separated was filtered off, washed with acetic acid and water, and recrystallized from 50% alcohol; 1.07 g of yellow crystals, m. p. 163-164°, were obtained. A mixed melting point test with the reduction product of 4-nitro-5,7-dibromobenzo-2,1,3-thiodiazole showed no depression.

b) Bromination in the fused state. To 1 g of fused 4-aminobenzo-2,1,3-thiodiazole, m. p. 68°, was added at 70-75° 1.1 ml of bromine, the mixture was boiled for 2 hours, after which it was cooled and the excess bromine evaporated; 2.35 g of a dark mass was obtained, which after recrystallization from 50% alcohol (in the presence of carbon) melted at 164°. A mixed melting point test with the bromination product of 4-aminobenzo-2,1,3-thiodiazole in acetic acid showed no depression.

5-Amino-6-chlorobenzo-2,1,3-thiodiazole. To 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116°, in 6 ml of acetic acid was added with stirring 0.83 g of dichloramine and then from a dropping funnel, gradually, a solution of 2 ml of concentrated hydrochloric acid in 4 ml of acetic acid. After 40 minute's stirring the precipitate that had separated was filtered off and washed consecutively with acetic acid and water. 0.89 g of material was obtained that melted after recrystallization from hot water at 152.5°. A mixed melting point test with the reduction product of 4-nitro-5-chlorobenzo-2,1,3-thiodiazole (m. p. 92°) showed a depression (92-102°).

Found %: N 22.74, 22.51; Cl 19.24, 19.32. $C_6H_4N_3SCl$. Calculated %: N 22.64; Cl 19.14.

5-Amino-6-bromobenzo-2,1,3-thiodiazole. To 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116° in 6 ml of acetic acid was added a solution of 0.4 ml of bromine in 6 ml of acetic acid over a period of 30 minutes at 20°. After 1 hour's stirring the precipitate that had separated was filtered off and washed with acetic acid and water. 1.46 g of crystals were obtained that melted after recrystallization from hot water at 126-127°. A mixed melting point test with the reduction product of 4-nitro-5-bromobenzo-2,1,3-thiodiazole (m. p. 114°) showed a depression (the mixture melted at 85-95°).

Found %: N 17.36, 17.18; Br 35.00, 34.65; S 12.87, 13.18. $C_6H_4N_3SBr$. Calculated %: N 18.26; Br 34.78; S 13.91.

Benzo-2,1,3-thiodiazole-4-thiourea. A mixture of 2.9 g of the hydrochloride of 4-aminobenzo-2,1,3-thiodiazole (obtained by saturation of an ether solution of the base with hydrogen chloride), 1.5 g of ammonium thiocyanate, and 50 ml of chlorobenzene was heated with stirring for 10 hours on a boiling water bath, after which the reaction mass was cooled and the precipitate was filtered off and washed consecutively with chlorobenzene and water. 1.85 g of a material was obtained that melted after recrystallization from 50% alcohol at 200° (with decomp.); yield 60%.

Found %: C 40.21, 39.89; H 3.31, 2.86; N 26.55, 26.29. $C_7H_6N_4S_2$. Calculated %: C 40.00; H 2.86; N 26.67.

7-Bromo-4,5-(2'-aminothiazole)benzo-2,1,3-thiodiazole. In a 50 ml three-necked flask fitted with a stirrer, reflux condenser, and dropping funnel were placed 0.85 g of benzo-2,1,3-thiodiazole-4-thiourea, m. p. 183°, and 100 ml of chloroform. To the mixture was added at 0° with stirring over a period of 45 minutes 1.5 g of bromine in 9 ml of chloroform, after which the reaction mass was stirred (at 0°) for another 75 minutes and then left overnight (the reaction was accompanied by evolution of hydrogen bromide). The precipitate was filtered off and washed with chloroform. 1.5 g was obtained of a material with an extended melting point. The reaction product was heated to boiling with a mixture of 50 ml of hydrochloric acid (d 1.19), 400 ml of water, and carbon, the hot solution was filtered, and an excess of 25% ammonia solution was added to the clear, hot filtrate. The precipitate that separated was filtered off and washed with water. Yellow crystals were obtained, m. p. 302° (with decomp.).

Found %: N 19.22, 19.64; Br 28.24, 27.93. $C_7H_3N_4S_2Br$. Calculated %: N 19.51; Br 27.87.

5,6-(2'-Aminothiazole)benzo-2,1,3-thiodiazole. 1) Benzo-2,1,3-thiodiazole-5-thiourea. a) A mixture of 2.75 g of the hydrochloride of 5-aminobenzo-2,1,3-thiodiazole (obtained by saturation of an ether solution of the base with dry hydrogen chloride), 1.5 g of ammonium thiocyanate, and 20 ml of chlorobenzene was heated with stirring on a boiling water bath for 8 hours; after cooling, the precipitate was filtered off and washed consecutively with chlorobenzene and water. 1.55 g was obtained of a material; m. p. 193° (with decomp.); yield ~60%.

b) A solution of 1 g of 5-aminobenzo-2,1,3-thiodiazole, m. p. 116°, and 1 g of potassium thiocyanate in 10 ml of hydrochloric acid (d 1.04) was heated on a boiling water bath for 15 hours. The reaction product (a liquid with a yellow precipitate) was concentrated, the residue was heated for 2 hours to 102-108°, cooled, treated with water, and the precipitate was filtered off and washed with water. 1.35 g of a material was obtained, m. p. 193° (with decomp.); yield almost quantitative. After recrystallization from 50% alcohol gray crystals were obtained, m. p. 200° (with decomp.).

Found %: C 39.53, 40.30; H 2.78, 2.95; N 26.43, 26.82. $C_7H_6N_4S_2$. Calculated %: C 40.00; H 2.86; N 26.27.

2) 5,6-(2'-Aminothiazole)benzo-2,1,3-thiodiazole. a) To a mixture of 0.55 g of benzo-2,1,3-thiodiazole-5-thiourea, m. p. 200° (with decomp.), and 7 ml of chloroform was added over the course of 45 minutes at 0° with stirring a solution of 0.5 g of bromine in 5 ml of chloroform (the reaction was accompanied by the evolution of hydrogen bromide), and stirring at 0° was continued for 2 hours more. The precipitate (0.85 g) was filtered off, washed with chloroform, boiled for 1/2 hour with a mixture of 90 ml of water, 10 ml of hydrochloric acid (d 1.19) and carbon, and the hot solution was filtered. To the hot solution was added an excess of ammonia solution. The precipitate that separated was filtered off and washed with water. After the crystals were dried, they melted at 261-262° and showed no depression with known material.

b) A solution of 0.75 g of 5-amino-6-bromobenzo-2,1,3-thiodiazole, m. p. 126-127°, in 50 ml of chlorobenzene was saturated with dry hydrogen chloride, and the excess of this was expelled with dry air. To a suspension of the hydrochloride that was formed was added 0.3 g of ammonium thiocyanate, and the mixture was heated on a boiling water bath for 8 hours (until the hydrogen bromide was removed). On cooling, the precipitate was filtered off, washed with chlorobenzene and water, boiled with a mixture of 90 ml of water, 10 ml of concentrated hydrochloric acid, and carbon, and the hot solution was filtered and treated with a solution of ammonia. The precipitate that separated was filtered off and washed with water. The crystals melted at 259-261° and showed no depression in a mixed melting point test with the material previously prepared.

4- and 5-Aminobenzo-2,1,3-thiodiazoles. a) 4-Aminobenzo-2,1,3-thiodiazole. 90 g of iron filings and 400 ml of water were heated to boiling, and 8 ml of 98% acetic acid and 26 g of 4-nitrobenzo-2,1,3-thiodiazole m. p. 105°, were added. After the mixture had been boiled with energetic stirring for 20 minutes and cooled, the precipitate (reaction product and iron sludge) was filtered off, washed with a small amount of water, and extracted with ether; 18.9 g of 4-aminobenzo-2,1,3-thiodiazole was obtained (87%), which after recrystallization from hot water melted at 68° [19].

b) 5-Aminobenzo-2,1,3-thiodiazole. Reduction of 5-nitrobenzo-2,1,3-thiodiazole, m. p. 127-128°, was carried out under conditions similar to the preceding; yield 85-87%, m. p. 116°. The product formed yellow needles, soluble in organic solvents and in hot water; solubility in the latter was higher than that of 4-aminobenzo-2,1,3-thiodiazole.

Found %: S 21.64; N 27.34. $C_6H_5N_3S$. Calculated %: S 21.19; N 27.61.

SUMMARY

1. It has been shown that upon chlorination of 4-aminobenzo-2,1,3-thiodiazole with dichloramine, 4-amino-5,7-dichlorobenzo-2,1,3-thiodiazole is formed in good yield; upon bromination of 4-aminobenzo-2,1,3-thiodiazole with bromine in acetic acid 4-amino-5,7-dibromobenzo-2,1,3-thiodiazole also is formed in good yield (80% and more).

2. It has been shown that 4-amino-5,7-dichloro- and 4-amino-5,7-dibromobenzo-2,1,3-thiodiazoles, respectively, are also formed by the treatment of fused 4-aminobenzo-2,1,3-thiodiazole with chlorine or bromine.

3. It has been shown that 5-amino-6-bromobenzo-2,1,3-thiodiazole is produced by the bromination of 5-aminobenzo-2,1,3-thiodiazole; by chlorination (with dichloramine) of 5-aminobenzo-2,1,3-thiodiazole, 5-amino-6-chlorobenzo-2,1,3-thiodiazole (supposedly) is produced.

4. It has been shown that when 4- and 5-aminobenzo-2,1,3-thiodiazoles are reacted with thiocyanic acid, benzo-2,1,3-thiodiazole-4-thiourea and benzo-2,1,3-thiodiazole-5-thiourea are formed, respectively, and are cyclized on bromination to the corresponding benzothiazole derivatives.

5. A practicable method has been found for the synthesis of 5,6-(2'-aminothiazole)benzo-2,1,3-thiodiazole both by the reaction of 5-amino-6-bromobenzo-2,1,3-thiodiazole with thiocyanic acid and by the bromination of benzo-2,1,3-thiodiazole-5-thiourea.

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Received January 17, 1957

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*Original Russian pagination. See C. B. Translation.

THE CHEMISTRY OF PROCESSES OF FAR-REACHING CHLORINATION OF PENTANE

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A number of investigators have studied the chlorination of pentane to mono- and disubstituted derivatives [1-6]. Very much less work has been devoted to the preparation of polychloropentanes containing more than two atoms of chlorine. Far-reaching chlorination of pentane has been effected photochemically [7] in a flow system in a medium of the reaction products (hexa- and heptachloropentanes). Reaction of tetrachloropentanes with chlorine has been studied at 370-500° under a pressure of some tens of atmospheres [8].

These conditions lead to considerable breakdown of the molecule. Chlorination of hexa-and heptachloropentanes has been studied at the ordinary pressure at 470° in an empty tube [7,9] as well as in a tube partly filled with infusorial earth impregnated with ferric chloride [10]. The temperature in the packed portion of the tube was 350-400° and that in the empty zone 450-500°. In both cases the main product of the reaction was hexachlorocyclopentadiene.

Formation of hexachlorocyclopentadiene on reaction of polychloropentanes with chlorine indicates that the carbon skeleton undergoes radical rearrangement with retention of the same number of carbon atoms. It has been suggested [7, 11] that chlorination, dehydrochlorination and cyclization take place in this case. The literature is lacking in experimental data concerning the mechanism of this process, which is also important for establishment of the theoretical bases of an industrial process of production of hexachlorocyclopentadiene. The latter is the principal intermediate for the production of a series of highly active insecticides, and it may find application in the industrial synthesis of other important compounds.

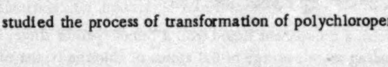
In the present work we studied the process of transformation of polychloropentanes into hexachlorocyclopentadiene.

Repetition of the literature methods of transformation of polychloropentanes into hexachlorocyclopentadiene led to formation of the desired product, of products of breakdown, and of an undistillable residue.

Study of these reaction products did not enable us to attack the problem of the mechanism of the processes involved since the use of a fairly high temperature allowed us to recover only the thermally stable compounds. We therefore made appreciable changes in the procedure for transformation of polychloropentanes. We chlorinated the latter in presence of infusorial earth at 350°. This caused a sharp fall in the yield of hexachlorocyclopentadiene but enabled the intermediate products to be isolated. Octachloropentadiene-1,3 and octachlorocyclopentene were found in the reaction mixture together with hexachlorocyclopentadiene and products of degradation. Formation of octachloropentadiene-1,3 evidently proceeds via nonachloropentenes and chlorination of polychloropentanes in alternating reactions of dehydrochlorination and addition of chlorine at the double bond.

The following scheme may be advanced for the conversion of polychloropentanes of normal structure into hexachlorocyclopentadiene:

$$C_5H_{12-n}Cl_n \xrightarrow{-(11-n)HCl} C_5HCl_9 \xrightarrow{-HCl} CCl_2{=}CCl{-}CCl{=}CCl{-}CCl_3 \rightarrow$$



Alternative schemes for conversion of polychloropentanes into hexachlorocyclopentadiene by a series of concurrent reactions can also be advanced. With the objective of checking the above scheme, we determined the material balance in the interaction of polychloropentanes with chlorine (see Table). In these experiments, which were run under various conditions, we obtained varying yields of reaction products, but we always observed a correspondence between the degrees of transformation of polychloropentanes as calculated from the carbon and hydrogen contents of the products.*

Degree of Transformation of Polychloropentanes ($C_5H_{5.5}Cl_{6.5}$) on Reaction with Chlorine, Calculated from the Carbon and Hydrogen Contents of the Reaction Products

Amt. polychloropentanes taken (g-moles)	HCl formed		Yield (%)						Deg. transformation polychloropentanes (%)	
	g-moles	g-moles/g-mole polychloropentane	CCl_4	C_2Cl_4	C_4Cl_6	C_5Cl_6	C_5Cl_8	cyclo-C_5Cl_6	from C	from H
1.112	5.34	4.79	0.9	1.4	2.5	20.6	6.5	55.5	87.4	87.0
0.556	2.61	4.70	0.9	0.5	7.0	21.6	10.7	46.9	87.6	85.5
1.112	5.27	4.74	0.9	2.6	2.1	29.2	2.8	50.4	88.0	86.0
1.112	5.42	4.86	1.1	3.8	5.6	30.6	5.0	40.6	86.7	88.5
1.112	5.20	4.66	1.3	4.2	1.9	60.4	3.5	11.7	83.0	85.0
0.556	2.09	3.75	0.4	1.6	11.7	32.2	15.0	8.2	69.1	68.4
0.400	1.92	4.80	3.6	0.7	1.5	45.0	16.7	16.8	84.3	87.0
1.112	5.10	4.69	0.4	1.3	8.3	53.7	12.2	12.6	88.5	83.5

Inspection of the table reveals a correspondence between the degrees of transformation of polychloropentanes calculated by the two independent methods. This correspondence indicates that we account for all of the main compounds formed in this process. The proposed scheme of transformations of polychloropentanes in presence of chlorine at high temperature is therefore the only one corresponding to the facts. Other possible schemes either do not apply or are realized to a negligible extent.

EXPERIMENTAL

Starting substances. Polychloropentanes were prepared by photochlorination of n-pentane. Constants of starting n-pentane: b. p. 36-37°, d_4^{20} 0.6252, n_D^{20} 1.3570.

Polychloropentanes form a transparent liquid with a lemon-yellow tinge; d_4^{20} 1.6584, n_D^{20} 1.5375; chlorine content 78%, corresponding to an average of 6.5 atoms of chlorine in the molecule.

Procedure. Chlorine was admitted from a cylinder via two flasks. The rate of flow of the chlorine was measured by a capillary flowmeter. Polychloropentanes were introduced from a dropping funnel. The reactor was a quartz tube, diameter 21 mm and length 1150 mm, filled with infusorial earth and placed in an electric furnace. Constant temperature was maintained in the furnace by means of a special system of regulating transformers. The temperature was measured with thermocouples. The reaction mixture entered a water condenser. Condensate formed was passed into a receiver, while the gases entered a trap maintained at −70°. An additional amount of liquid products of reaction collected in the trap. The gases passed from the trap into two columns (in series) for collection of hydrogen chloride and chlorine.

Analysis of the products of reaction. The hydrogen chloride content of the aqueous solutions was determined. The organic products of reaction were decanted and fractionally distilled in a flask fitted with a Vigreux column. At the start the chlorine and hydrogen chloride were eliminated by air-blowing at room temperature; after this, vacuum fractionation was carried out. We give the results of fractional distillation of the products of reaction in one experiment. 323 g of reaction mixture gave 9 g (2.8%) of chlorine and hydrogen chloride; the following liquid fractions were obtained:

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* The degree of transformation of the carbon of polychloropentanes was determined as the sum of the yields of chlorocarbons formed. The degree of transformation of the hydrogen of polychloropentanes was determined as the ratio of the quantity of hydrogen chloride actually evolved in the process to the maximum quantity of hydrogen chloride that can be released on the assumption of exhaustive chlorination of the starting substances. Hydrogen was substantially absent from the organic products of transformation of polychloropentanes.

1st, 3.5 g (1.1%), up to 82° (200 mm), d_4^{20} 1.6158, n_D^{20} 1.5038; 2nd, 16.4 g (5.1%) 82-110° (200 mm), d_4^{20} 1.6713, n_D^{20} 1.5370; 3rd, 8.5 g (2.6%), 110-112° (35 mm), d_4^{20} 1.6920, n_D^{20} 1.5568; 4th, 99.5 g (30.8%), 92-95° (4.5 mm), d_4^{20} 1.7044, n_D^{20} 1.5645; 5th, 36.7 g (11.4%), 95-100° (4.5 mm), d_4^{20} 1.7112, n_D^{20} 1.5655; 6th, 18.2 g (5.6%), 105-123° (4.5 mm), d_4^{20} 1.7447, n_D^{20} 1.5668; 7th, 11.9 g (3.7%), 123-125° (4.5 mm), d_4^{20} 1.7876, n_D^{20} 1.5720; 8th, 99.6 g (30.8%), 125-126° (4.5 mm), d_4^{45} 1.8064, n_D^{45} 1.5671; residue 11.6 g (3.6%).

The 7th fraction was subjected to further fractionation. The substance isolated had the constants: m. p. −77°, b. p. 100-102° (1.5 mm), d_4^{20} 1.7732, n_D^{20} 1.5708; these correspond to the literature data for octachloro-1,3-pentadiene [12]: m. p. −78°, b. p. 117° (3 mm), d_{15}^{25} 1.7664, n_D^{20} 1.5700.

Found %: C 17.8; Cl 82.1. C_5Cl_8. Calculated %: C 17.5; Cl 82.5.

Octachloro-1,3-pentadiene was passed together with chlorine through a reaction tube at 350° filled with infusorial earth. The main product of the reaction was octachlorocyclopentene (yield 75%); a small quantity of hexachlorocyclopentadiene (yield 9%) was also formed. It is known [14] that octachloro-1,3-pentadiene isomerizes (cyclizes) at a moderate temperature (up to 100°) to octachlorocyclopentene in presence of aluminum chloride.

The 8th fraction was recrystallized from alcohol. The compound isolated had the constants: m. p. 39°, b. p. 117° (3 mm), d_4^{45} 1.8189, n_D^{45} 1.5679, corresponding to the literature data for octachlorocyclopentene [12]: m. p. 38°, b. p. 107° (1.6 mm), 134° (6 mm), d_{15}^{45} 1.816, n_D^{45} 1.5683.

Found %: C 17.8; Cl 82.3. C_5Cl_8. Calculated %: C 17.5; Cl 82.5.

The isolated substance was passed through an empty tube at 500° to give hexachlorocyclopentadiene, an equimolar quantity of chlorine and unchanged starting substance. It is known [12, 13] that at 325-500° octachlorocyclopentene changes into hexachlorocyclopentadiene. The same process also takes place in the absence of catalyst at temperatures above 260° [15].

SUMMARY

1. Reaction of polychloropentanes of normal structure with chlorine was effected under conditions permitting isolation of the main intermediate products of transformation of the starting compounds into hexachlorocyclopentadiene. Under these conditions octachloro-1,3-pentadiene and octachlorocyclopentene were isolated and identified.

2. It was shown that the transformation of polychloropentanes into hexachlorocyclopentadiene proceeds according to the scheme: polychloropentanes → nonachloropentenes → octachloro-1,3-pentadiene → octachlorocyclopentene → hexachlorocyclopentadiene.

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Received January 7, 1957

THE REACTION OF PHOSPHORUS PENTACHLORIDE WITH ESTERS OF OXAMIC ACID

AMIDES OF ALKOXYDICHLOROACETIC ACIDS

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As was shown earlier [1], the action of phosphorus pentachloride on ethyl oxamate (oxamethane) gives in succession the amide of ethoxydichloroacetic acid and trichlorophosphazoethoxydichloroacetyl according to the equations

$$C_2H_5OCOCONH_2 + PCl_5 \longrightarrow POCl_3 + C_2H_5OCCl_2CONH_2 \qquad (1)$$

$$C_2H_5OCCl_2CONH_2 + PCl_5 \longrightarrow 2HCl + C_2H_5OCCl_2CON{=}PCl_3 \qquad (2)$$

The preparation of trichlorophosphazoethoxydichloroacetyl and its analogs has been studied fairly closely and it has been shown that reaction (2) is a general one for the synthesis of trichlorophosphazoalkoxydichloroacetyls [2]. It was of interest to establish whether reaction (1) is a general one and whether it can be utilized as a general method of preparation of amides of alkoxydichloroacetic acids.

It was found that reaction (1) goes with adequate speed at temperatures very much lower than in the case of reaction (2) for the methyl, ethyl, butyl and isobutyl esters of oxamic acid. This enabled us to obtain good yields of the corresponding alkoxydichloroacetic acids, although in all cases reaction (2) proceeds side by side with reaction (1). Quantitative separation of the amides of alkoxydichloroacetic acids and trichlorophosphazoalkoxydichloroacetyls is impossible, but the quantity of trichlorophosphazo compound formed can be estimated with facility from the quantity of hydrogen chloride evolved whose determination is remarkably simple. It was found that reaction (1) in the case of butyl and isobutyl esters of oxamic acid goes with a yield of about 90% at a temperature of -10 to -5° in the course of 20-30 minutes. Very little hydrogen chloride is evolved. Reaction of ethyl oxamate with phosphorus pentachloride according to equation (1) takes place only at a very much higher temperature (8 to 10°) in the course of 50-60 minutes, and the yield is about 70%. The reaction is accompanied by evolution of about 10% of hydrogen chloride according to equation (2). Methyl oxamate reacts with phosphorus pentachloride with even greater difficulty. At 10° the reaction takes 3 hours and is accompanied by release of about 20% of hydrogen chloride according to equation (2). The yield of amide of methoxydichloroacetic acid is only 60-64%. Consequently, reaction (1) proceeds the most sluggishly in the case of methyl oxamate, more easily with ethyl oxamate, and very easily with the butyl and isobutyl esters.

Amides of dichloroaroxyacetic acids could not be obtained from aryl esters of oxamic acid [3] (phenyl, tolyl, p-chlorophenyl, p-nitrophenyl and naphthyl). Reaction of 1 mole of phosphorus pentachloride and 1 mole of aryl esters of oxamic acid gives a mixture of the corresponding trichlorophosphazoaroxydichloroacetyl and unreacted aryl ester of oxamic acid. The result is the same if less phosphorus pentachloride is used, but more of the ester of oxamic acid remains unchanged. Consequently, equation (2) goes more rapidly than (1) in the case of aryl esters of oxamic acid, and therefore this scheme cannot lead to amides of aroxydichloroacetic acids.

The practical impossibility of obtaining amides of aroxydichloroacetic acids may be due either to slowing down of reaction (1) or to acceleration of reaction (2), or to both of these causes. It is well-known that the oxygen atom linked to carbon by a weakly polarized double bond (in aldehydes, ketones and esters of oxalic acid) is relatively easily replaced by two atoms of chlorine under the action of phosphorus pentachloride [4]. Under the same conditions the oxygen atom linked to the carbon atom by a very much more strongly polarized double bond (in esters of carboxylic and many other acids) is not replaced by two atoms of chlorine. Consequently, increased polarization of a double bond $>C=O$ undoubtedly hinders the replacement of an oxygen atom by two chlorine atoms under the action of phosphorus pentachloride. The probable reason is that polarization of a carbon−oxygen double bond hinders the formation of an intermediate product of addition of the $[PCl_4]^+$ ion to the oxygen atom, since the $>C=\overset{+}{O}-PCl_4$ grouping (unpolarized $>C=O$ bond) is more advantageous than the $>\overset{+}{C}-O-PCl_4$ grouping (polarized $>\overset{+}{C}-\overset{-}{O}$ bond). Isomerization of one grouping into the other is hindered by the same forces that promote polarization.

On the other hand, experiment shows that the rate of formation and, in particular, the stability of trichlorophosphazo compounds increase with increasing strength of the acid corresponding to the original amide. For example, the amide of trichloroacetic acid is readily converted into the exceptionally stable trichlorophosphazo compound [5]; a very much less stable trichlorophosphazo compound is obtained with greater difficulty from the amide of p-nitrobenzoic acid, a still less stable product is obtained from benzamide [6], and no product at all is obtained from acetamide. Replacement of alkyl by aryl in esters of oxamic acid is bound to increase the polarization of the double bond of $>C=O$ in the ROCO− group; on the other hand replacement of alkyl by aryl must slow down reaction (1) and accelerate reaction (2), thus eliminating the possibility of formation of amides of aroxydichloroacetic acids as intermediates of the reaction. The same causes must accelerate reaction (1) and slow down reaction (2) on passing from methyl oxamate to higher aliphatic esters (observations confirm this), since methyl is the most electronegative of all the unsubstituted alkyls. However, the increase in yields of amides of alkoxydichloroacetic acids on transition from lower esters of oxamic acid to higher is also the consequence of the considerably lower stability of methoxydichloroacetamide in comparison with the amides of higher alkoxydichloroacetamides. This behavior is not due to the same cause, i.e., lowering of the electronegativity on transition from methyl to higher amides, but it makes clear why methyl and ethyl chlorides are split off very easily, while chlorobenzene is hardly ever split off.

Amides of alkoxydichloroacetic acids are colorless, crystalline substances with melting points higher than those of the corresponding trichlorophosphazoalkoxydichloroacetyls [2]. They are hydrolyzed by moist air with relative facility but with considerably greater difficulty than trichlorophosphazoalkoxydichloroacetyls. The halogen atoms in amides of alkoxydichloroacetic acids are very labile and are easily replaced by various groups. Heating of amides of alkoxydichloroacetic acids leads to their breakdown with formation of alkyl halides, hydrogen chloride, and solid products whose nature has not yet been established. Decomposition of amides of methoxy- and ethoxydichloroacetic acids is quantitative at relatively low temperatures (60-100°):

$$C_2H_5OCCl_2CONH_2 \longrightarrow C_2H_5Cl + HCl + C_2O_2NH$$

The solid substance obtained in the reaction is probably the product of further transformations of the initially formed oxalic acid imide or oxalic acid half nitrile.

Amides of butoxydichloroacetic acids decompose with incomparably greater difficulty when heated, due undoubtedly to the considerably greater facility of cleavage of methyl and ethyl chlorides in comparison with higher alkyl chlorides.

For this reason the amides of methoxy- and ethoxydichloroacetic acids are extraordinarily difficult to obtain in the pure state. They begin to split off alkyl halide with appreciable speed even at 60°, and they partly decompose during recrystallization. The results of nitrogen determinations on amides of methoxy- and ethoxydichloroacetic acids are therefore a little on the high side (see Experimental), while chlorine determinations on ethoxydichloroacetamide give results that are much too low, since decomposition of the substance by water or alkali solution causes a portion of the chlorine to volatilize as ethyl chloride. Results of analyses of amides of butoxy- and isobutoxydichloroacetic acids are in adequate agreement with the theoretical values.

The structure of the amides of alkoxydichloroacetic acids is fully confirmed by their reaction with phenols [3] according to the equation $NH_2COCCl_2OR + ArOH \longrightarrow NH_2COCOOAr + HCl + RCl$

and by the transformation of methoxydichloroacetamide into diphenoxymethoxyacetamide (yield about 75%) according to the equation $CH_3OCCl_2CONH_2 + 2NaOC_6H_5 \rightarrow 2NaCl + CH_3OC(OC_6H_5)_2CONH_2$

EXPERIMENTAL

All of the starting substances and the solvents used for the syntheses described below must be thoroughly purified.

Methoxydichloroacetamide (I). Twenty-five ml of carbon tetrachloride and 0.1 mole of finely pulverized methyl oxamate were placed in a flask fitted with a stirrer and thermometer and attached to a reflux condenser which was connected in succession to a small bubble counter containing a few drops of sulfuric acid and a hydrogen chloride trap containing 250 ml of water. The mixture was cooled to 5°, 0.1 mole of finely pulverized phosphorus pentachloride was added quickly, the stirrer was started, and the temperature was held at 8-10°. (Since at lower temperatures the reaction goes extremely slowly, while at higher temperatures the quantity of liberated hydrogen chloride is sharply reduced [reaction (2) is accelerated]). The phosphorus pentachloride gradually goes into solution, hydrogen chloride is slowly evolved, and (I) soon starts to come out of solution in the form of colorless scales. The reaction is completed in 3 hours. This is indicated by the disappearance of the yellow grains of phosphorus pentachloride and by cessation of evolution of hydrogen chloride. 0.03-0.04 mole of hydrogen chloride in all was liberated or 15-20% of the quantity calculated from equation (2). (I) was suction-filtered, washed with ligroine (2 × 3 ml) and dried in vacuo at room temperature. Yield 9-10 g (60-64%); m. p. 95-96°. After recrystallization from benzene (9 g 50 ml, heating for only a short period), the melting point and elementary composition did not change.

Found %: N 9.78, 9.48. Equiv. after hydrolysis 2.70, 2.78. $C_3H_5O_2NCl_2$. Calculated %: N 8.90. Equiv. after hydrolysis 3.00.

The substance is slowly hydrolyzed by water at room temperature and rapidly on boiling; it is very easily soluble in dioxane and acetone, easily soluble in dichloroethane; it can be recrystallized, with partial decomposition, from benzene and carbon tetrachloride; it is sparingly soluble in boiling ether and ligroine.

Thermal cleavage of (I). (I) slowly splits off methyl chloride when kept in vacuo at room temperature. The reaction is much faster at 60°, while at 100° it is completed in 2 hours and 86% of the methyl chloride comes off (b. p. -24°).

Conversion of (I) into phenyl oxamate. See [3].

Conversion of (I) into diphenoxymethoxyacetamide (monomethyl-diphenyl orthoester of oxamic acid) (II). To a mixture of 0.04 mole of sodium phenate and 50 ml of benzene was added 0.02 mole of (I) with vigorous stirring. The reaction goes with liberation of heat. After 30 minutes the mixture was heated to the boil, and the separated sodium chloride was filtered off. On cooling, the solution deposited (II) in the form of colorless, fine crystals. M. p. 157-159° after recrystallization from benzene. Yield 70-73%. (II) is tasteless and odorless, insoluble in water and 0.1 N alkali, sparingly soluble in boiling carbon tetrachloride and ligroine; it can be recrystallized from alcohol, ether and benzene.

Found %: N 5.26, 5.08. $C_{15}H_{15}O_4N$. Calculated %: N 5.13.

Ethoxydichloroacetamide (III) was prepared in the same manner as (I). At 8-10° the reaction is completed in 50-60 minutes. About 10% of hydrogen chloride is released, calculated on equation (2). The reaction solution deposited 10-10.5 g of (III) with m. p. 80-82°. The mother liquor yielded a further 1-1.5 g of (III) after evaporation in vacuo at room temperature to a volume of 10 ml. Further evaporation leads to separation from the liquor of the secondary reaction product – trichlorophosphazoethoxydichloroacetyl. Total yield of (III) about 70%. M. p. 81-82° after recrystallization from carbon tetrachloride (10 g from 35 ml with only short-period heating); the composition was unchanged.

Found %: N 8.36, 8.40, 8.34, 8.53. Equiv. after hydrolysis 2.82, 2.84 (phenolphthalein); 1.90, 2.03 (methyl orange). $C_4H_7O_2NCl_2$. Calculated %: N 8.15. Equiv. after hydrolysis 3.00 (phenolphthalein), 2.00 (methyl orange).

Results of chlorine determinations (after hydrolysis with warm water) were 4-5% low.

(III) crystallizes in the form of fine, colorless prisms scarcely differing from (I) in solubility, but easily soluble in benzene and carbon tetrachloride. Heating to above 60° for several hours leads to quantitative breakdown of (III) into 1 mole of ethyl chloride, 1 mole of hydrogen chloride, and a solid substance of unknown structure. Treatment with phenols gives the corresponding esters of oxamic acid [3].

Butoxydichloroacetamide (IV). The reaction is completed in 20 minutes at a temperature of -5 to -10°; very little hydrogen chloride is released. (IV) goes completely into solution when the reaction mixture is brought to room temperature. After filtration through a dry filter, the solution was evaporated in vacuo (5 mm) at 30-40°. The residue contained (IV) in the form of a viscous oil which soon crystallized completely. Yield 90%; after recrystallization from ligroine (b. p. 90-95°), (IV) is obtained in the form of long, colorless needles; m. p. 57-59°. It is appreciably more soluble in common solvents than (III).

Found %: N 7.19, 7.36; Cl 35.00, 34.97. Equiv. after hydrolysis 3.11, 3.09. $C_6H_{11}O_2NCl_2$. Calculated %: N 7.00; Cl 35.48. Equiv. after hydrolysis 3.00.

Isobutoxydichloroacetamide (V) was obtained in the same manner as (IV). Yield 90%; it crystallizes from ligroine in the form of needles up to 10 mm in length; m. p. 76-78°. It hardly differs from (IV) in solubility.

Found %: Cl 35.41, 35.30. Equiv. after hydrolysis 3.07, 3.04. $C_6H_{11}O_2NCl_2$. Calculated %: Cl 35.48. Equiv. after hydrolysis 3.00.

Reaction of equimolar quantities of phosphorus pentachloride and aromatic esters of oxamic acid was studied with many substances under a great diversity of reaction conditions. In no case could the amides of the corresponding aroxydichloroacetic acids be obtained. These experiments are therefore not described in detail.

SUMMARY

Reaction of equimolar quantities of phosphorus pentachloride and aliphatic esters of oxamic acid gives amides of alkoxydichloroacetic acids. Amides of the corresponding aroxydichloroacetic acids could not be isolated from the products of reaction of phosphorus pentachloride with aromatic esters of oxamic acid.

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Received November 20, 1956

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* Original Russian pagination. See C. B. Translation.

DIESTERS OF ARYLAMIDOPHOSPHORIC ACIDS

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By analogy with diesters of arylsulfonamidophosphoric acids [1] diesters of arylamidophosphoric acids ought to be formed by the action of sodium arylates or alcoholates on the diacid chlorides of arylamidophosphoric acids according to scheme (1), or by saponification of triaroxyphosphazoacyls according to scheme (2).

$$\mathrm{ArCONHPOCl_2 + 2NaOR \longrightarrow 2NaCl + ArCONHPO(OR)_2} \qquad (1)$$

$$\mathrm{ArCON{=}P(OR)_3 + H_2O \longrightarrow ROH + ArCONHPO(OR)_2} \qquad (2)$$

The dimethyl ester of benzoylamidophosphoric acid is obtained according to scheme (1) in presence of excess of sodium methoxide and methyl alcohol in yield of 87%, but aromatic diesters are obtained by the same scheme (from dry phenolates) in yields not exceeding 10-25%. Changes in the reaction conditions, including the use of 3 moles of phenolate instead of 2, do not improve the yields. The reason for this is unknown, since the corresponding diesters of alkyl- and arylsulfonamidophosphoric acids are obtained by a similar scheme in very good yields [1].

Scheme (2) leads to very satisfactory yields of diaryl esters, and there is no need to isolate the easily saponified triaroxyphosphazoacyls [2]. We can start directly from trichlorophosphazoacyls [3] which react with dry sodium arylates in benzene, ether or dioxane solutions to give the corresponding triaroxyphosphazoacyls [2] according to the scheme

$$\mathrm{ArCON{=}PCl_3 + 3NaOR \longrightarrow 3NaCl + ArCON{=}P(OR)_3}$$

Without separation of the precipitated sodium chloride, water is added to the resultant solution of triaroxyphosphazo compound, and the mixture is refluxed.

Triaroxyphosphazoacyls are hydrolyzed to diesters with incomparably greater facility than triaroxyphosphazosulfonaryls [1], and 5-10 minutes' heating with water is sufficient for complete transformation of triaroxyphosphazoacyls into diaryl esters of acylamidophosphoric acids.

p-Chlorobenzonitrile is sometimes isolated as a by-product in the preparation of diesters of p-chlorobenzoylamidophosphoric acid; it is formed by thermal cleavage of triaroxyphosphazo-p-chlorobenzoyls [2] or of diaryl esters of p-chlorobenzoylamidophosphoric acid; this cleavage process evidently goes parallel with reaction (2).

Scheme (2) gave the methyl, phenyl, p-cresyl, p-chlorophenyl and o- and p-nitrophenyl esters of benzoyl-, p-chlorobenzoyl- and p-nitrobenzoylamidophosphoric acids and the di-α-naphthyl ester of benzoylamidophosphoric acid.

All of the diesters, with the exception of the nitrophenyl esters, are colorless crystalline substances, melting in the range of 116-196°, insoluble in water, sparingly soluble in ether and ligroine, easily soluble in benzene, acetone, chloroform and dioxane. The aromatic diesters can be recrystallized from alcohol, carbon tetrachloride, and ligroine. The dimethyl esters are readily soluble in alcohol and can be recrystallized from water, carbon tetrachloride and mixtures of benzene and ligroine.

Dinitrophenyl esters of acylamidophosphoric acids are colorless or faint-yellow crystalline substances, melting over the range of 151-180°, insoluble in water and common organic solvents except dioxane. They can be recrystallized from a mixture of dioxane and alcohol.

All of the diesters of acylamidophosphoric acids are monobasic acids. The dimethyl esters titrate exactly in presence of phenolphthalein in aqueous solutions; all of the others, except the nitrophenyl esters, titrate in aqueous alcoholic or alcoholic solutions. Only the dimethyl esters dissolve easily in aqueous solutions of caustic alkalies; all of the others are very sparingly soluble due to the poor solubility of the salts. The nitro esters could not be titrated because the solutions of their salts are very strongly colored. Heating of the nitro esters with aqueous alcoholic caustic alkali brings them into solution, and the sodium salts of the diesters come down, after cooling, in the form of brightly colored needles. On treatment with dilute acids, these salts are transformed into the original dinitrophenyl esters.

EXPERIMENTAL

Dimethyl benzoylamidophosphate (I). To a cooled solution of 0.03 mole of sodium methoxide in 15 ml of methanol was added portionwise 0.01 mole of pulverized diacid chloride of benzoylamidophosphoric acid (II). Addition of each portion was marked by strong heat development or even by boiling up of mixture. After the whole of the (II) had been added, the mixture was refluxed for 15 minutes, after which the methanol was evaporated in vacuo. The residue was dissolved in water, and the solution was filtered and acidified with hydrochloric acid. (I) came down in the form of colorless platelets; yield 87%; m. p. 116-117°; the m. p. rose to 116-118° after recrystallization from a 1:1 mixture of benzene and ligroine or from 20% aqueous alcohol.

Found %: N 6.01. Equiv. 1.050. $C_9H_{12}O_4NP$. Calculated %: N 6.11. Equiv. 1.000.

Di-p-cresyl benzoylamidophosphate (III). To 0.04 mole of finely pulverized, thoroughly dried sodium cresylate was added 50 ml of dry dioxane and 0.02 mole of (II). Heat was developed on mixing. The reaction mixture was refluxed for 15 minutes, the dioxane was distilled off in vacuo, the residue was treated with water for removal of sodium chloride, and the precipitated oil was separated and dissolved in 80% alcohol with heating. On cooling, (III) came down in the form of colorless plates; yield 26%; m. p. 146-147°.

Found %: N 3.51. $C_{21}H_{20}O_4NP$. Calculated %: N 3.67.

(III) is obtained in 33.8% yield when (II) is heated with sodium cresylate in 1:3 molar ratio in benzene solution.

Di-p-chlorodiphenyl benxoylamidophosphate (IV) was obtained in the same manner as (III); colorless needles; yield 28.5%; m. p. 131-133°

Found %: N 3.26. $C_{19}H_{14}O_4NCl_2P$. Calculated %: N 3.31.

Di-p-nitrodiphenyl benzoylamidophosphate (V) was obtained in the same manner as (III); light-yellow prisms; m. p. 151-152°.

Found %: N 9.41. $C_{19}H_{14}O_8N_3P$. Calculated %: N 9.48.

Diphenyl benzoylamidophosphate (VI). To thoroughly dried and finely pulverized sodium phenolate (0.01 mole) was added in one portion a solution of 0.033 mole of trichlorophosphazobenzoyl in 80 ml of benzene. After the violent reaction had subsided, the mixture was refluxed with vigorous stirring for 15 minutes, after which 25 ml of water was added and the stirred mixture was boiled for another 5 minutes. On cooling, the benzene layer was separated, washed once with water, and filtered; the benzene was distilled off in vacuo. The residue contained an oily liquid which was dissolved in 5 ml of ether. (VI) quickly came down and was suction-filtered and washed with ether. It formed colorless needles after recrystallization from a 1:1 mixture of ligroine and ether; yield 65.1%; m. p. 147-149°.

Found %: N 3.96. Equiv. 1.002, 1.013. $C_{19}H_{16}O_4NP$. Calculated %: N 3.97. Equiv. 1.000.

Esters (III), (VII), (IV), (VIII)-(XIII), described below, were prepared in the same manner as (VI).

Di-p-cresyl benzoylamidophosphate (III); yield 52.4%; colorless plates after recrystallization from alcohol; m. p. 146-147°; no melting point depression in admixture with (III) obtained from (II).

Di-α-naphthyl benzoylamidophosphate (VII); yield 55.6%; sparingly soluble in cold benzene and therefore starts to come down even on washing of the benzene solution with water. Recrystallization from benzene gives tablets with m. p. 195-196°.

Found %: N 3.39. $C_{27}H_{20}O_4NP$. Calculated %: N 3.09.

Di-p-chlorophenyl benzoylamidophosphate (IV); yield 75.6%; it forms plates with m. p. 131-133° from a mixture of benzene and ligroine; no melting point depression in admixture with (IV) prepared from (II).

Diphenyl p-chlorobenzoylamidophosphate (VIII). When the synthesis is performed in benzene solution, p-chlorobenzonitrile is obtained as residue after the benzene has been distilled off; m. p. 94-95° [4]. Evidently, triphenoxyphosphazo-p-chlorobenzene or (VIII) is completely decomposed in boiling benzene solution. The yield is 34.4% when the synthesis is performed in a medium of ether, but an appreciable quantity of p-chlorobenzonitrile is then also obtained at the same time. Colorless prisms with m. p. 142-143° after recrystallization from alcohol.

Found %: N 3.85. $C_{19}H_{15}O_4NClP$. Calculated %: N 3.61.

Di-p-cresyl ester of p-chlorobenzoylamidophosphoric acid (IX); yield 31.3% (in benzene solution); colorless needles from alcohol; m. p. 139-140°.

Found %: N 3.53. $C_{21}H_{19}O_4NClP$. Calculated %: N 3.57.

Di-p-chlorodiphenyl p-chlorobenzoylamidophosphate (X); yield 74%; needles with m. p. 155-156° from alcohol.

Found %: N 3.18. $C_{19}H_{13}O_4NCl_3P$. Calculated %: N 3.07.

Diphenyl p-nitrobenzoylamidophosphate (XI); yield 89.1%; crystallizes from carbon tetrachloride or alcohol in the form of slender, light-yellow needles; m. p. 151-152°.

Found %: N 6.97. Equiv. 1.004, 0.958. $C_{19}H_{15}O_6N_2P$. Calculated %: N 7.04. Equiv. 1.000.

Di-p-cresyl p-nitrobenzoylamidophosphate (XII); yield 54.6%; light-yellow prisms from alcohol with m. p. 165-167°.

Found %: N 6.53. $C_{21}H_{19}O_6N_2P$. Calculated %: N 6.58.

Di-p-chlorodiphenyl p-nitrobenzoylamidophosphate (XIII); yield 79.5%; yellow prisms from alcohol; m. p. 175-176°.

Found %: N 6.03. $C_{19}H_{13}O_6N_2Cl_2P$. Calculated %: N 6.00.

Di-o-nitrodiphenyl benzoylamidophosphate (XIV). 0.02 mole of (II) was added quickly to a mixture of thoroughly dried sodium o-nitrophenate and 50 ml of dry benzene. Slight heat was generated on mixing. The stirred reaction mixture was boiled until nearly the whole of the nitrophenate had disappeared (about 1 hour). 25 ml of water was then added, and boiling and stirring were continued for another few minutes. After 24 hours, the precipitated (XIV) was suction-filtered, washed with water, alcohol and ether for removal of nitrophenol, and dried. Yield 90.7%. The product was purified by dissolution in a small volume of hot dioxane, filtration of the solution, and addition to it of twice the volume of alcohol. Light-yellow prisms came down on cooling; m. p. 154-155°.

Found %: N 9.53. $C_{19}H_{14}O_8N_3P$. Calculated %: N 9.48.

The esters (V), (XV)-(XVIII) were prepared in the same way as (XIV).

Di-p-nitrodiphenyl benzoylamidophosphate (V); yield 66%; light-yellow prisms from a mixture of dioxane and alcohol; m. p. 151-152°; no depression in admixture with (V) obtained from (II).

Di-o-nitrodiphenyl p-chlorobenzoylamidophosphate (XV); yield 62%; light-yellow needles; m. p. 179-180°.

Found %: N 8.70. $C_{19}H_{13}O_8N_3ClP$. Calculated %: N 8.80.

Di-p-nitrodiphenyl p-chlorobenzoylamidophosphate (XVI); yield 57.8%; light-yellow prisms; m. p. 167-168°.

Found %: N 8.93. $C_{19}H_{13}O_8N_3ClP$. Calculated %: N 8.80.

Di-o-nitrodiphenyl-p-nitrobenzoylamidophosphate (XVII); yields 84.6%, light-yellow prisms, m. p. 178-179°.

Found %: N 11.61. $C_{19}H_{13}O_{10}N_4P$. Calculated %: N 11.47.

Di-p-nitrodiphenyl p-nitrobenzoylamidophosphate (XVIII); yield 81.7%; light-yellow needles; m. p. 179-180°.

Found %: N 11.25. $C_{19}H_{13}O_{10}N_4P$. Calculated %: N 11.47.

Dimethyl benzoylamidophosphate (I). 0.025 mole of trichlorophosphazobenzoyl was added in small portions to a solution of 0.1 mole of sodium methoxide in 30 ml of methanol while cooling. The reaction was violent. After the whole of the trichlorophosphazobenzoyl had been added, the methyl alcohol was taken off in vacuo, the residue was dissolved in water, and the solution was filtered and acidified with hydrochloric acid. (I) came down as colorless plates; yield 56.5%; m. p. 116-118°. No change in melting point after recrystallization from 20% alcohol. No depression of melting point in admixture with (I) prepared from (II).

Esters (XIX) and (XX) were obtained from the corresponding trichlorophosphazoacyls in the same manner as (I).

Dimethyl p-chlorobenzoylamidophosphate (XIX); yield 90.9%; needles from 10% alcohol with m. p. 125-126°.

Found %: N 5.80. Equiv. 1.023. $C_9H_{11}O_4NClP$. Calculated %: N 5.92. Equiv. 1.000.

Dimethyl p-nitrobenzoylamidophosphate (XX); yield 87.3%; light-yellow needles from 50% alcohol with m. p. 153-154°.

Found %: N 10.19. $C_9H_{11}O_6N_2P$. Calculated %: N 10.22.

SUMMARY

A study was made of the reaction of diacid chlorides of arylamidophosphoric acids and of trichlorophosphazoacyls with sodium methoxide and sodium arylates. A series of diesters of arylamidophosphoric acids were prepared and their properties described.

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Received November 26, 1956

PREPARATION OF 2,4-DINITROPHENYL DERIVATIVES OF HYDROXY AND MERCAPTO COMPOUNDS AND AMINES

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The recommended procedure for the preparation of 2,4-dinitrophenyl derivatives for identification of hydroxy and mercapto compounds [1] is treatment of the latter with 2,4-dinitrochlorobenzene or 2,4-dinitrofluorobenzene in presence of various alkaline agents such as caustic alkalies [2, 3], sodium bicarbonate [4, 5], triethylamine [6] and a few other agents [7]. 2,4-Dinitrophenyl derivatives of amines are obtained by the interaction of equivalent quantities of amine and 2,4-dinitrochlorobenzene [1].

We showed earlier that 2,4-dinitrochlorobenzene reacts with hydroxy compounds in presence of anhydrous potassium fluoride with formation of ethers of 2,4-dinitrophenol [8]. It was found that the corresponding fluoro derivative (2,4-dinitrofluorobenzene) reacts with hydroxy compounds more smoothly in presence of anhydrous potassium fluoride than in presence of other bases. In this case the reaction goes from start to finish in a substantially neutral medium. In the case of primary alcohols and phenols, the pure 2,4-dinitrophenyl derivatives are obtained directly from the reaction mass in yields approaching the theoretical. The reaction goes according to the equation:

$$R{-}OH + F{-}C_6H_3(NO_2)_2 + KF \rightarrow R{-}O{-}C_6H_3(NO_2)_2 + KHF_2$$

2,4-Dinitrophenyl derivatives of secondary hydroxy compounds are obtained in better yields in presence of of anhydrous potassium fluoride than in presence of the usually employed triethylamine. For example, the 2,4-dinitrophenyl derivative of N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline is obtained in 79% yield in presence of potassium fluoride, while in a parallel experiment using triethylamine the yield is only 28%. The 2,4-dinitrophenyl derivative of phenylmethyl carbinol is obtained in 28% yield with potassium fluoride (in a secondary reaction 12% of 2,2',4,4'-tetranitrodiphenyl ether is formed), whereas in presence of triethylamine the yield is only 11%. In this case the main product of the reaction is 2,2',4,4'-tetranitrodiphenyl ether (43%) whose formation is evidently due to the water liberated [8] by dehydration of phenylmethyl carbinol.

The literature [4] mentions that 2,4-dinitrophenol does not react with 2,4-dinitrofluorobenzene. 2,4-dinitrophenol and 2,4-dinitrofluorobenzene react in presence of potassium fluoride to give a substantially quantitative yield of 2,2',4,4'-tetranitrodiphenyl ether. p-Hydroxybenzoic acid gives a good yield of 2,4-dinitrophenyl derivative. The 2,4-dinitrophenyl derivative of salicylic acid could not be obtained. This contrasts with the behavior of its methyl ester.

Mercapto compounds are quantitatively converted into the 2,4-dinitrophenyl derivatives when heated with 2,4-dinitrochlorobenzene in presence of potassium fluoride. Products of adequate purity are obtained directly from the reaction mass.

$$R{-}SH + Cl{-}C_6H_3(NO_2)_2 + 2KF \rightarrow R{-}S{-}C_6H_3(NO_2)_2 + KCl + KHF_2$$

Primary mercaptans react with 2,4-dinitrofluorobenzene even at room temperature in presence of potassium fluoride. 2,4-Dinitrophenyl derivatives of secondary mercaptans are obtained in somewhat lower yields. These derivatives are not easily obtained in the crystalline form, in agreement with the literature [3]. In the absence of potassium fluroide, 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene do not react with mercapto compounds.

2,4-Dinitrophenyl derivatives of amines, prepared by reaction with 2,4-dinitrochloro- and 2,4-dinitrofluorobenzene in presence of potassium fluoride, are directly isolated from the reaction mass in the analytically pure form and in substantially quantitative yield.

Such a weakly basic amine as 2,4-dinitroaniline reacts with 2,4-dinitrochloro- and 2,4-dinitrofluorobenzene in presence of potassium fluoride at 120-130° to give 2,2',4,4'-tetranitrodiphenylamine in substantially quantitative yield (it was previously obtained in poor yield by heating 2,4-dinitrobromobenzene at 160° with 2,4-dinitroaniline in nitrobenzene in presence of potassium carbonate, potassium iodide and copper) [12].

The 2,4-dinitrophenyl derivative is quantitatively formed from anthranilic acid by the action of 2,4-dinitro derivative of both chlorobenzene and fluorobenzene in presence of potassium fluoride.

EXPERIMENTAL

Preparation of 2,4-dinitrophenyl derivatives of hydroxy compounds. 0.0025 mole of hydroxy compound was heated and stirred with the equivalent (0.47 g) of 2,4-dinitrofluorobenzene and 0.29 g (0.005 mole) of potassium fluoride [8] at 100-110°. The reaction mass was treated with hot benzene and filtered. The benzene was distilled off on a water bath, and the residue dissolved in a small quantity of boiling alcohol from which the 2,4-dinitrophenyl ether came down on cooling. Products so obtained are of adequate purity and their melting points as a rule are not raised after recrystallization (Table 1).

Reaction of N-phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline with 2,4-dinitrofluorobenzene in presence of triethylamine. 0.57 g of the hydroxy compound was heated (with stirring) for 5 hours with 0.47 g of 2,4-dinitrofluorobenzene and 3 drops of triethylamine at 100-110°. Crystallization of the reaction mixture from alcohol gave 0.27 g (28%) of derivative with m. p. 124°. A mixture with the product obtained in presence of potassium fluroide (m. p. 126°) melts at 124.5°.

Reaction of phenylmethyl carbinol with 2,4-dinitrofluorobenzene. 1) 1.22 g of phenylmethyl carbinol, 1.86 g of 2,4-dinitrofluorobenzene and 1.16 g of potassium fluoride were stirred for 2 hours at 140-150°. The reaction mass was treated with hot benzene and filtered. The benzene was driven off and the residue recrystallized from alcohol to give 0.21 g (12%) 2,2'4,4'-tetranitrodiphenyl ether (poorly soluble in hot alcohol) with m. p. 193° and 0.81 g (28%) of 2,4-dinitrophenyl derivative of phenylmethyl carbinol with m. p. 99°; the latter crystallizes as light-yellow needles.

Found %: N 9.82, 9.93. $C_{14}H_{12}N_2O_5$. Calculated %: N 9.71.

2) 0.43 g of phenylmethyl carbinol and 0.64 g of 2,4-dinitrofluorobenzene were stirred with 4 drops of triethylamine for 2 hours at 140-150°. The reaction mass was recrystallized from alcohol to give 0.26 g (43%) of 2,2',4,4'-tetranitrodiphenyl ether with m. p. 193° and 0.11 g (11%) of the 2,4-dinitrophenyl derivative of phenylmethyl carbinol with m. p. 97°. A mixture with the product obtained in the preceding experiment had m. p. 98°.

Reaction of 2,4-dinitrophenol with 2,4-dinitrofluorobenzene. 0.46 g of 2,4-dinitrophenol, 0.47 g of 2,4-dinitrofluorobenzene and 0.58 g of anhydrous potassium fluoride were stirred at 190-200° with 2 g of 2,4-dinitrochlorobenzene for 3 hours. The reaction mass was treated with hot water and filtered. The precipitate was repeatedly washed on the filter with water, then 3 times with alcohol (2 ml each time). In this manner 0.86 g (98%) of faintly yellowish, finely crystalline powder was obtained with m. p. 194.5°. The literature reports m. p. 195° [9]. A mixture with an authentic specimen of 2,2',4,4'-tetranitrodiphenyl ether did not give a depression of melting point.

Reaction of p-hydroxybenzoic acid with 2,4-dinitrofluorobenzene. 0.7 g of p-hydroxybenzoic acid, 0.93 g of 2,4-dinitrofluorobenzene and 0.58 g of potassium fluoride were stirred for 3 hours at 120-130°. The reaction mass turned yellow and towards the end of the experiment it solidified. The product was pulverized and washed with water, with hydrochloric acid (1 : 1) and twice with alcohol (2 ml each time). The product was purified by reprecipitation with water from 3 ml of concentrated sulfuric acid to give 1.4 g (93%) of substance with m. p. 254°. The melting point remained unchanged after recrystallization from acetic acid.

Found %: N 8.90, 9.03. $C_{13}H_8O_7N_2$. Calculated %: N 9.20.

Preparation of 2,4-dinitrophenyl derivatives of mercapto compounds. 0.0025 mole of mercapto compound was heated for 10-15 minutes at 100° with 0.51 g (0.0025 mole) of 2,4-dinitrochlorobenzene and 0.29 g (0.005 mole) of potassium fluoride. Ten ml of hot benzene was added to the reaction mass, and the mixture was filtered. The benzene was driven off on a water bath, and the residue was dissolved in a small quantity of boiling alcohol from which, on cooling, pure 2,4-dinitrophenyl derivative was deposited as yellow crystals (Table 2).

Reaction of n-butylmercaptan with 2,4-dinitrofluorobenzene. 0.23 g of n-butylmercaptan was stirred with 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of potassium fluoride. After a few minutes, the reaction mass turned yellow and solidified. Further treatment was similar to that described above. Yield 0.55 g (86%) of derivative with m. p. 66°.

TABLE 1

Reaction of Hydroxy Compounds with 2,4-Dinitrofluorobenzene

Hydroxy compound	Reaction period (hours)	% yield	Melting point	
			found	literature data
Ethyl alcohol*	1	93	85°	85° [6]
n-Octadecyl alcohol	5	81	65.5	65.5 [8]
1-Naphthol	0.5	97	127	128 [2]
2-Naphthol	0.5	93	94	95 [2]
p-Isooctylphenol	0.5	95	94.5 **	—
o-Hydroxydiphenyl	0.5	99	113 ***	—
p-Hydroxydiphenyl	0.5	95	116	118 [2]
Methyl salicylate	1	95	89	88 [7]
N-Phenyl-3-hydroxy-1,2,3,4-tetrahydroquinoline	5	79	126 ****	—

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*Reaction was performed in excess of boiling alcohol (10 moles).

**White needles. Found %: N 7.52, 7.64. $C_{20}H_{24}O_5N_2$. Calculated %: N 7.53.

***White needles. Found %: N 8.29, 8.23. $C_{18}H_{12}O_5N_2$. Calculated %: N 8.32.

****Orange plates. Found %: N 10.75, 10.85. $C_{21}H_{17}O_5N_3$. Calculated %: N 10.73.

Reaction of sec-butylmercaptan with 2,4-dinitrofluorobenzene. 0.32 g of sec-butylmercaptan was stirred with 0.65 g of 2,4-dinitrofluorobenzene and 0.4 g of potassium fluoride for an hour at 90-100°. Further treatment was similar to that described above. Yield 0.61 g (69%) of product with m. p. 67.5°. The compound was isolated in the form of an oil which crystallized only after several days.

Found %: N 11.00, 10.85. $C_{10}H_{12}O_4N_2S$. Calculated %: N 10.92.

Preparation of 2,4-dinitrophenyl derivatives of amines. 1) 0.93 g of amine, 2.03 g of 2,4-dinitrochlorobenzene and 1.16 g of potassium fluoride were heated for 30 minutes at 100°; the solidified reaction mass was then pulverized, washed with water, with 5% hydrochloric acid again with water until the filtrate was free from chlorine ion, and finally with 2 ml of methyl alcohol. Yield 2.5 g (97%) with m. p. 156°. The literature [1] reports m. p. 156°. In a parallel experiment run without potassium fluoride, the product had m. p. 128-130°. The pure product could only be obtained by recrystallization from alcohol.

The same procedure for reaction of p-toluidine with 2,4-dinitrochlorobenzene in presence of potassium fluoride gave a product with m. p. 135°. The literature [1] reports m. p. 136°. In the absence of potassium fluoride the product had m. p. 116-120°.

2) 0.36 g of α-naphthylamine, 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of anhydrous potassium fluoride were heated for 10-15 minutes at 100°. Further treatment was on the same lines as described above. Yield 0.77 g (99%) of product with m. p. 191°. Literature: m. p. 191° [1].

The 2,4-dinitrophenyl derivative of β-naphthylamine was obtained in similar fashion. Yield 0.75 g (97 %); m. p. 173° (the literature reports m. p. 179° [10] and m. p. 171° [11]). The melting point was unchanged after recrystallization from 1 : 1 mixture of benzene and alcohol.

Reaction of 2,4-dinitroaniline with 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene. 1) 0.46 g of 2,4-dinitroaniline was stirred with 0.51 g of 2,4-dinitrochlorobenzene and 0.29 g of potassium fluoride for 2.5 hours at 120-130°. The reaction mass turned red and solidified. The product was pulverized and washed with hot water. The color changed from red to yellow. Yield 0.85 g (97%). Recrystallization from aqueous acetone gave lustrous yellow plates with m. p. 199.5°. Literature: m. p. 199° [12].

2) Replacement of 2,4-dinitrochlorobenzene by 0.47 g of 2,4-dinitrofluorobenzene gave under the same conditions 0.86 g (99%) of product with m. p. 200° after recrystallization from aqueous acetone.

Reaction of anthranilic acid with 2,4-dinitrochlorobenzene. 0.34 g of anthranilic acid was stirred for 30 minutes with 0.51 g of 2,4-dinitrochlorobenzene and 0.29 g of potassium fluoride at 120-130°. The reaction mass turned red and solidified. The product was pulverized, washed with water and treated with 10% hydrochloric acid, after which it was washed many times with water and finally twice with methanol (2 ml each time). Yield 0.69 g (91%) with m. p. 259°. It formed yellow-needles, m. p. 262.5°, after recrystallization from a mixture of methyl alcohol and acetone. Literature: m. p. 262° [13].

0.34 g of anthranilic acid, 0.47 g of 2,4-dinitrofluorobenzene and 0.29 g of potassium fluoride similarly gave 0.74 g (97.5%) of product with m. p. 262°.

TABLE 2

Reaction of Mercapto Compounds with 2,4-Dinitrochlorobenzene

Mercapto compound	Yield of derivatives (%)	Melting point of derivatives	
		found	literature data [3]
p-Thiocresol	98	102.5°	103°
Thiophenol	97	120	121
p-Chlorothiophenol	97	123	123
n-Butylmercaptan	97	63	66

SUMMARY

A procedure for the preparation of 2,4-dinitrophenyl derivatives of hydroxy and mercapto derivatives and amines was developed; it consisted of treatment with 2,4-dinitrochlorobenzene and 2,4-dinitrofluorobenzene in presence of potassium fluoride.

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Received January 8, 1957

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*Original Russian pagination. See C. B. Translation.

RADIOCHEMICAL INVESTIGATION OF REACTIONS OF ORGANOMETALLIC COMPOUNDS IN BENZENE SOLUTION

I. A. Korshunov and A. A. Orlova*

With the help of deuterated benzene, G. A. Razuvaev, G. G. Petukhov, A. F. Rekasheva and G. P. Mikluk-hin [1] showed that diphenylmercury and phenylmercuric hydroxide behave differently in benzene solutions when irradiated with ultraviolet light. Whereas diphenylmercury reacts in the solvent a definitely radical mechanism with regeneration of the phenyl radicals, phenylmercuric hydroxide initially forms a reaction coil with the solvent.

In the present work a radiochemical method was used in a study of the behavior of diphenylmercury and phenylmercuric hydroxide in benzene solutions on photolysis and heating. Employment of a radiochemical procedure excluded the possibility of errors associated with hydrogen exchange between organometallic compounds and deuterated benzene. A radiochemical label in the form of radiocarbon was introduced into the benzene used as the reaction medium. Radioactive benzene was synthesized by the method of N. D. Zelinskii [2] from labeled acetylene prepared in turn from labeled barium carbide [3].

The activity of the original benzene and of the reaction products was determined with the help of an internally filled counter (carbon dioxide) [4]. The organic compound was previously burned to CO_2 in an oxygen stream using a micro method. Activities were measured with an accuracy of up to 3%.

A weighed sample of about 0.5 g of organometallic compound and 3-4 ml of labeled benzene with a specific activity of the order of 1.4×10^5 pulses/min. were placed in a quartz test tube which was then sealed and exposed to the light from a quartz mercury lamp. The period of irradiation varied between 50 and 150 hours. Thermal decomposition was effected in the same test tubes at 170-190° for 70-130 hours.

The reaction products were fractionated by the procedure previously recommended in a study of the photolysis of diphenylmercury and diphenylmercuric hydroxide in deuterated benzene. In a number of experiments the photolysis and thermal breakdown were not continued to the stage of complete breakdown of the starting organometallic compounds. These conditions permitted detection of the activity in the original diphenylmercury and diphenylmercuric hydroxide that indicated occurrence of exchange between these compounds and the solvent (benzene). In these cases the degree of exchange was determined in relation to the original activity after allowing for dilution.

Since diphenyl is formed in the process of breakdown of organometallic compounds, it was necessary to check for the absence of exchange by phenyl radicals between diphenyl and labeled benzene. Investigation of the system diphenyl—benzene under drastic conditions showed that exchange of radicals does not occur. Results of a series of experiments on photolysis and thermal breakdown in the system diphenylmercury—labeled benzene are presented in Table 1.

We see from the data of Table 1 that benzene participates in the photolysis and thermal breakdown of diphenylmercury. Passage of activity into diphenyl is of the order of 20-25%, which is in good agreement with the conclusions of the authors of the paper on the radical character of the reactions cited above.

In formation of an intermediate reaction coil, the activity of the resultant diphenyl should actually be higher due to its uniform distribution between diphenylmercury and benzene. In the event of incomplete

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*M. A. Chernyshev and K. I. Vereshchagin participated in the experimental work.

TABLE 1

Photolysis and Thermal Breakdown of Diphenylmercury in Labeled Benzene (Activity of the original benzene 250 pulses/min; volume of counter tube 25 ml; CO_2 pressure 45 mm)

Reaction conditions	Reaction duration (hours)	Activity (pulses/min)		% exchange
		of benzene after reaction	of diphenyl	
Irradiation with light	50	185	50	20.0
	50	182	51	20.4
	100	196	58	23.2
	100	188	61	24.4
	150	192	60	24.0
	150	189	59	23.8
Heating to 170°	70	195	58	23.2

TABLE 2

Photolysis and Thermal Breakdown of Phenylmercuric Hydroxide in Labeled Benzene (Volume of counter tube 25 ml; CO_2 pressure 45 mm)

Reaction conditions	Reaction duration (hours)	Activity (pulses/min)		% exchange
		of original benzene	of diphenyl	
Irradiation with light	120	330	150	45.5
	100	568	300	52.8
Heating to 170°	75	568	266	46.8

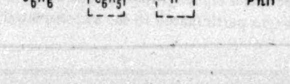
decomposition of the diphenylmercury, a part of the activity appears in the latter. Passage of activity into diphenylmercury is the consequence of the reversibility of the breakdown of diphenylmercury to radicals:

$$\mathrm{PhHg}\cdot + \overset{\bullet}{\mathrm{C}}_6\mathrm{H}_5 \rightleftarrows \mathrm{PhHg}\overset{\bullet}{\mathrm{C}}_6\mathrm{H}_5$$

The maximum transition of activity into diphenylmercury was 10%, but it was usually about 3-4%. Experimental data for the photolysis and thermal breakdown of phenylmercuric hydroxide in benzene are given in Table 2.

As we thus see from Table 2, photolysis and thermal breakdown of phenylmercuric hydroxide results in about 50% of the activity of the benzene passing into the product of breakdown (diphenyl). The presence of considerable activity in phenylmercuric hydroxide was simultaneously detected during its incomplete decomposition. In some experiments this transition of activity was of the order of 23-25%.

It seems to us that the high degree of passage of activity into phenylmercuric hydroxide testifies to formation of a reaction coil whose reversible dissociation leads to transition of activity from the benzene into the hydroxide [1]:



It should be noted that thermal breakdown of phenylmercuric hydroxide results in formation of considerably more insoluble products of decomposition with higher activity than in the case of photolysis.

The same method was employed for the photolysis of tetraphenyllead in benzene solution. The investigations revealed the absence of exchange by phenyl-radicals in this system in the absence of catalysts.

The authors are extremely grateful to G. A. Razuvaev and G. G. Petukhov for their help and counsel.

SUMMARY

1. With the help of carbon-labeled benzene the previously advanced mechanism of photolysis and thermal breakdown of diphenylmercury and phenylmercuric hydroxide was confirmed.

2. It was established that exchange does not occur in the systems diphenyl—benzene and tetraphenyllead—benzene.

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Gorkii State University Received December 29, 1956

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RADIOCHEMICAL DETERMINATION OF THE NUMBER OF CARBON ATOMS IN AN ORGANIC MOLECULE

I. A. Korshunov and N. F. Novotorov

In studies by a number of authors [1-4] internally filled counters have been employed for the determination of activity of compounds containing the radioactive isotope C^{14}. Determination of the activity of labeled compounds is possible when they are directly introduced into the counter tube [4] or in the form of carbon dioxide obtained after combustion of the organic compound in an oxygen stream. Errors of measurement by this procedure do not exceed ±1%. The high efficiency of the count and the relatively low background value enables counts of low specific activities to be made.

In the present work we demonstrate the possibility of using an internally filled counter for determining the number of carbon atoms in an organic molecule and for determination of the purity of a labeled compound.

We denote by a_g the specific activity of carbon dioxide obtained after combustion of a labeled organic compound (in pulses/min. per mmole); the activity of the labeled compound itself before combustion will be denoted by a_p (pulses/min. per mmole). The ratio a_p/a_g evidently gives the number of carbon atoms in the labeled organic compound corresponding to one radioactive carbon atom in the same compound. The reciprocal ratio a_g/a_p defines the proportion of active carbon atoms (C^{14}) relative to the total number of carbon atoms in the investigated compound.

The specific activity of a specimen is equal to the measured activity of the specimen A and the number of millimoles of compound in the specimen, i.e.:

$$a = A \cdot \frac{RT}{pv}, \tag{1}$$

where p is the partial pressure of the labeled compound, v is the volume of the counter tube, and T is the temperature (°K).

Since T and v were constant in the experiments, we can write the following expression for the specific activity

$$a = k \cdot \frac{A}{p}, \tag{2}$$

from which we have:

$$\frac{a_n}{a_g} = \frac{A_n \cdot p_g}{A_g \cdot p_n} \tag{3}$$

In the presence of a "pure" organic compound and a known number of labeled carbon atoms, equation (3) can be used to find the total number of carbon atoms in the investigated compound from the measured activities at given pressures in the counter tube. But if the composition of the compound is known, then the deviation of the ratio a_p/a_g from the theoretically calculated value enables us to judge the degree of purity of the organic compound.

For a mixture of two pure organic compounds, one of which contains radioactive carbon atoms, the molar proportion of radioactive compound γ is:

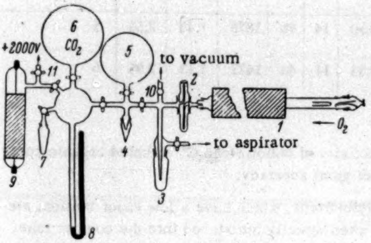
$$\gamma=\frac{a_n}{a_g}\cdot\frac{1}{\nu}, \qquad (4)$$

where v is the total number of carbon atoms in both of the molecules of the organic compounds.

With the help of the last expression we can find the quantitative composition of a mixture of organic substances.

For our experimental work we synthesized a variety of labeled organic compounds. These included unsaturated hydrocarbons [5] which were prepared by dehydration of labeled alcohols over kaolin catalyst at 400-420°. The olefins were subjected to chromatographic purification. The alcohols [6, 7] were prepared by reduction of esters of 1-C^{14} carboxylic acids with lithium aluminum hydride; alkylbenzenes were prepared by alkylation of benzene with labeled olefins; esters [7] were prepared by esterification of 1-C^{14} carboxylic acids with alcohol; organic acids were prepared by carboxylation with labeled carbon dioxide of organometallic compounds of lithium [8] and magnesium [9].

The radiochemical investigations were conducted in the apparatus illustrated in the drawing. The main component of the counter mixture was carbon dioxide. The organic compound was subjected to microcombustion [10] its activity was measured in the form of $C^{14}O_2$; this combustion was effected in a quartz tube (see drawing). The carbon dioxide was purified with anhydrone in trap 2 and frozen in trap 3 before being transferred to counter tube 9. The background activity was measured with ordinary carbon dioxide prepared from sodium carbonate and sulfuric acid. The CO_2, purified by freezing in traps 2 and 3, was placed in bulb 6. Test tube 7 contained 5-10 ml of anhydrous ethyl alcohol; the alcohol was used as a quenching additive when the tube was charged for determination of the background. Test tube 4 and bulb 5 were filled with volatile organic compounds whose activities had been determined. The manometer 8 was used for proportioning the counter mixture. The accuracy of reading of the pressure was improved with the help of a special cathetometer with a vernier scale graduated in 0.05 mm divisions. Measurements were performed in an AMM-4 type of counter tube 9 with a copper cathode. The working voltage of the tube was 1800-2000 V. The length of the plateau was 200-300 V with a slope of 0.5% per 100 V. The apparatus was connected up at junctions 10 and 11 in vacuo.

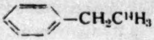
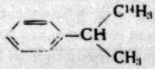


Apparatus for radiochemical determination of carbon C^{14}. Explanation in text.

For all of the investigated compounds the length and slope of the plateau of the counter characteristic were determined in dependence on the composition of the mixture; in addition, the relation between the rate of counting and the quantity of labeled substance introduced into the counter was measured, and the reproducibility of the results after a recharge with the same substance was determined.

Measurements were carried out over a period that ensured a statistical error of not more than 1%. The accuracy of determination of the labeled compounds in an internally filled counter was found to be ± 1% for measurements on specimens of carbon dioxide after allowing for the quadratic error and errors in measurements of pressure, etc. In the case of vapors of liquid organic substances the errors increased to 2-10%. The latter depends upon the vapor tension of the compounds introduced into the counter tube. The composition of the counter components, results of measurement of activity of the investigated compounds, and calculations from the formulas are presented in the table.

Results of Measurement of Activity of Labeled Compounds. (Temperature 20°, total pressure in counter tube 60 mm)

Compound investigated	Organic compound				Carbon dioxide				Total carbon atoms, labeled molecule	
	part. pressure in counter mixture (mm)		activity		part. pressure in counter mixture (mm)		activity			
	P_p of C^{14} compound	CO_2	a_p (pulses/min.)	$a_p \times 10^{-4}$ (pulses/min.)/mmole	ethyl alcohol	P_g of $C^{14}O_2$	A_g (pulses/min.)	$a_p \times 10^{-4}$ (pulses/min.)/mmole	found	calculated
$CH_3C^{14}H_2OH$	14	46	897	2.34	14	46	1451	1.16	2.02	2
$CH_3C^{14}OOCH_3$	14	46	912	2.38	14	46	1022	0.81	2.93	3
$CH_3C^{14}OOC^{14}H_2CH_3$	14	46	988	2.60	14	46	1598	1.28	4.08	4
$CH_3CH_2C^{14}H_2OH$	10	50	806	2.92	14	46	1264	1.00	2.93	3
$CH_3CH_2C^{14}OOCH_3$	15	45	1080	2.63	14	46	820	0.65	4.05	4
$CH_3CH_2C^{14}OOC^{14}H_2CH_3$	15	45	1520	3.69	14	46	1836	1.46	5.08	5
$C^{14}H_2=CH \cdot CH_3$	15	45	3231	7.85	14	46	3340	2.65	2.96	3
$CH_3CH_2CH_2C^{14}OOCH_3$	10	50	1920	7.00	14	46	1738	1.38	5.08	5
$CH_3CH_2CH_2C^{14}OOC^{14}H_2CH_3$	8*	46	1820	8.30	14	46	3556	2.82	5.88	6
	4*	46	1935	17.60	14	46	2898	2.29	7.68	8
	1*	50	1169	43.00	14	46	5480	4.36	9.8	9
$\Sigma C^{14}H_3=CHCH_3$ and $CH_2=CH_2$ (1 : 1)	15	45	1590	3.80	14	46	1878	1.49	2.56	5
$\Sigma CH_3C^{14}H_2OH$ and $CH_3COOC_2H_5$ (1 : 1)	14	46	1278	3.33	14	46	1422	1.13	2.95	6

Our investigations showed that the determination of activity of radioisotope C^{14}-labeled organic compounds possessing a high vapor tension can be performed with great accuracy.

Organic compounds, such as isopropylbenzene and ethylbenzene, which have a low vapor tension, are quantitatively determined with a lower degree of accuracy when directly introduced into the counter tube. An increase in accuracy necessitates preliminary combustion of the compound and conversion into carbon dioxide. The resultant dilution causes the activity per unit of gas pressure in the counter tube to be lowered in proportion to the number of carbon atoms in the burned molecule (Equation 3). The number of carbon atoms in the investigated organic molecules found from these relations and the theoretically calculated values are presented in the Table. The deviation of the experimental values from those calculated, after allowing for experimental errors, permits of quantitative evaluation of the purity of the compounds in question. It follows from the two last experiments that $\gamma = \frac{1}{2}$; consequently the original active vapor undergoes twofold dilution with the inactive component, and this actually occurs.

SUMMARY

1. The possibility was shown of utilizing the internally filled counter for radiometric measurement of active carbon dioxide and of organic compounds with a vapor tension under normal conditions of not less than 4-5 mm mercury column. The labeled compound can be at the same time a quenching additive.

2. Comparison of the activities when counting the labeled C^{14} compound in the form of vapor and carbon dioxide after combustion permits of determination of the total number of carbon atoms in a molecule and of the proportion of isotopic carbon atoms in the same molecule, as well as of quantitative evaluation of the presence of impurities in an organic compound.

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Received December 24, 1956

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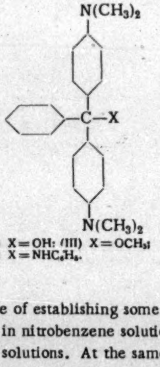
* Original Russian pagination. See C. B. Translation.

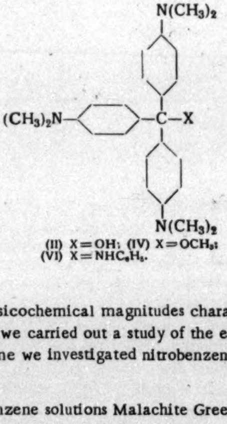
THE PROBLEM OF THE DISSOCIATION OF ARYLCARBINOLS AND SOME OTHER COMPOUNDS IN NITROBENZENE. I.

E. I. Kviat and O. F. Ginzburg

It is well known that in nitrobenzene solutions bis-(p-dimethylaminophenyl)-phenylcarbinol (I) and tris-(p-dimethylaminophenyl)-carbinol (II) slowly undergo progressive dissociation with formation of cations of the dyes Malachite Green and Crystal Violet [1, 2]. Our experiments have shown that similar transformations accompanied by formation of cations of dyes are undergone by the methyl esters of aminotriphenyl carbinols (III and IV) and by the so-called amino bases of triphenylmethane dyes (V and VI) in which the central carbon atom is linked to an amino group.



(I) X=OH; (III) X=OCH$_3$;
(V) X=NHC$_6$H$_5$.

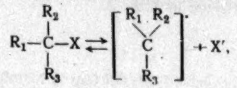


(II) X=OH; (IV) X=OCH$_3$;
(VI) X=NHC$_6$H$_5$.

With the objective of establishing some physicochemical magnitudes characterizing the state of the above-noted substances in nitrobenzene solutions, we carried out a study of the electrical conductivity and optical density of these solutions. At the same time we investigated nitrobenzene solutions of iodides of Malachite Green (VII) and Crystal Violet (VIII).

Our experiments have shown that in nitrobenzene solutions Malachite Green and Crystal Violet behave like strong electrolytes. On the basis of the data presented in the Experimental part (Table 5), the equivalent electrical conductivities of nitrobenzene solutions of these dyes at infinite dilution were found by graphical extrapolation. The equivalent electrical conductivity at infinite dilution of a nitrobenzene solution of Malachite Green iodide was found to be $\lambda^{\infty} = 26.5\,\Omega^{-1}\,\text{cm}^2$, and that of Crystal Violet iodide was $= 25.5\,\Omega^{-1}\,\text{cm}^2$.

Entirely different relations are observed in a study of the electrical conductivity of nitrobenzene solutions of compounds with a covalent structure. In the first place it should be noted that the electrical conductivity of such nitrobenzene solutions only rises gradually and in the majority of cases it is considerably lower than the conductivity of solutions of dyes of the same concentration. Moreover, dilution of solutions of covalent compounds causes the electrical conductivity to fall disproportionately with the change of concentration. These data, together with the results of a spectrophotometric study of nitrobenzene solutions, show that the slow dissociation that we have studied and which may be represented by the scheme:



$$R_1-\overset{R_2}{\underset{R_3}{C}}-X \rightleftarrows \left[\overset{R_1\;R_2}{\underset{R_3}{C}}\right]^{\cdot} + X',$$

increases with dilution. On the basis of the data obtained in spectrophotometric measurements (see Table 8) we succeeded in calculating the degree of dissociation of compounds of the Malachite Green group. The values are given in Table 1.

Starting from the values obtained for the degree of dissociation and the magnitudes of the electrical conductivity of solutions of these compounds (Table 7), it was found possible to calculate the limiting equivalent electrical conductivities of nitrobenzene solutions of compounds (I), (III) and (V); these values are given in Table 1.

TABLE 1

Degree of Dissociation and Limiting Equivalent Electrical Conductivity of Derivatives of Malachite Green

Compound	c (moles/liter)	α (%)	λ°
(I)	$1.6 \cdot 10^{-4}$	21	23.5
(III)	$1.6 \cdot 10^{-4}$	25	23.5
(V)	$8 \cdot 10^{-5}$	57	21

On the basis of the experimental data of Walden [3], we calculated the limiting equivalent electrical conductivity of the iodide ion in nitrobenzene solution and obtained a value of $\lambda^{\circ} = 20\Omega^{-1}\ cm^2$. On the basis of this value and of the values of equivalent electrical conductivity at infinite dilution for Malachite Green iodide, we obtained a value characterizing the limiting equivalent electrical conductivity of cations of Malachite Green in nitrobenzene solutions. This also enabled us to determine the magnitude of the limiting electrical conductivity in nitrobenzene for the OH', OCH_3' and NHC_6H_5' ions. The data so obtained are given in Table 2 (column 2).

Study of nitrobenzene solutions of compounds (II), (IV) and (VI) with a concentration of $1.6 \cdot 10^{-5}$ molar showed that the optical density of such solutions is identical. These data testify to the fact that under the conditions indicated above compounds (II) and (IV) are completely dissociated into cations of the dye and the corresponding anions. An attempt was therefore made to determine the limiting electrical conductivity of compounds (II) and (IV) by the extrapolation method. The same value of $\lambda^{\circ} = 23.5\Omega^{-1}\ cm^2$ was obtained for both of the compounds. Electrical conductivities of the OH' and OCH_3' ions calculated with the help of this value are presented in Table 2 (column 3). We see that the values of limiting electrical conductivity obtained by different methods are in very satisfactory agreement, while the mobilities of OH' and OCH_3' ions are somewhat higher then the mobility of the NHC_6H_5' ion, probably due to the larger volume of the NHC_6H_5' ion in comparison with OH' and OCH_3' ions. At the same time, the data indicate an extremely low mobility of hydroxyl ions in nitrobenzene (nearly 10 times lower than in water); this is evidently due to the mechanism of migration of ions in nitrobenzene being different from the mechanism in aqueous solutions.

Limiting equivalent electrical conductivities of compounds (II), (IV) and (VI) were calculated on the basis of the data of Table 2. The value found for (II) and (IV) was $\lambda^{\circ} = 23\Omega^{-1}\ cm^2$, and that for (VI) was $\lambda^{\circ} = 20\Omega^{-1}\ cm^2$.

The degree of dissociation of the above-described compounds in nitrobenzene solutions was also determined, using the approximation method of Debye and Onsager [4] and the tables of Schedlovsky [5]. The degree of dissociation was calculated from the electtical conductivity values found on the 30th day after preparation of the solutions. Results are presented in Table 3.

TABLE 2

Limiting Electrical Conductivities of Ions in Nitrobenzene Solutions

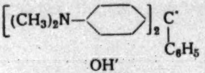
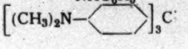
Ions	From data obtained in a study of compounds of the group (λ°)		Mean value of λ°
	of Malachite green	of Crystal violet	
1	2	3	4
	6.5	—	—
OH'	17.0	18.0	17.5
OCH_3'	17.0	18.0	17.5
NHC_6H_5'	14.5	—	—
	—	5.5	—

TABLE 3

Degree of Dissociation of Some Electrolytes in Nitrobenzene

c (moles/liter)	Degree of dissociation α (%)							
	(VIII)	(II)	(IV)	(VI)	(VII)	(I)	(III)	(V)
$1 \cdot 10^{-2}$	94.1	3.7	6.1	7.1	96.4	1.4	1.1	3.8
$2 \cdot 10^{-3}$	96.2	12.1	27.7	—	97.8	3.5	3.1	8.8
$4 \cdot 10^{-4}$	97.2	51	63.3	75.1	99.7	8.6	9.6	21.5
$8 \cdot 10^{-5}$	98.2	99.2	100	100	100	—	—	—
$1.6 \cdot 10^{-5}$	100	100	100	—	—			

The dissociation constants and the isobaric potentials of formation ΔZ° were calculated for the iodides of Crystal Violet and Malachite Green, as well as for compounds (I), (III) and (V), by extrapolation (with some degree of approximation) by means of the formula of Debye and Onsager [6]. Results appear in Table 4, from which it is evident that compounds (I) and (III) have the same dissociation constants in nitrobenzene and that the constant is only one-tenth of the dissociation constant of compound (V).

It should be noted that the dissociation constant of compounds (II), (IV) and (VI) could not be calculated from the data presented in Table 3. This shows that equilibrium was not attained in all of the solutions that we studied. The probable reason is that in some nitrobenzene solutions these compounds undergo other transformations in addition to dissociation. This theory is supported by our observation of change of color and fall in electrical conductivity in nitrobenzene solutions of compounds (II), (IV) and (VI) with a concentration of $4 \cdot 10^{-4}$ molar and higher after standing for 30 days.

EXPERIMENTAL

The specific electrical conductivity of the nitrobenzene employed as solvent ranged between $1.6 \cdot 10^{-7}$ and $1.8 \cdot 10^{-7}\ \Omega^{-1}\ cm^{-1}$.

An amplifier designed according to the data of Luder [7] was included in a standard circuit for measurement of electrical conductivity. Measurements were performed at 25°± 0.05°. The instrument constant K was 0.117. The specific electrical conductivity values in the tables have been corrected for the electrical conductivity of nitrobenzene itself.

TABLE 4

Dissociation Constants and Isobaric Potentials

	Substance				
	(VIII)	(VII)	(I)	(III)	(V)
K	0.1	0.1	$1 \cdot 10^{-6}$	$1 \cdot 10^{-6}$	$1 \cdot 10^{-5}$
$\Delta Z^o \left(\frac{\text{kcal}}{\text{mole}}\right)$	1360	1360	8200	8200	6800

The SF-11 spectrophotometer was used for the spectrophotometric measurements.

All of the investigated compounds were synthesized according to the literature data [8-12].

Malachite Green (VII) and Crystal Violet (VIII). The electrical conductivity of nitrobenzene solutions of these dyes, taken in the form of iodides [4], remained constant with time. Values are presented in Table 5.

TABLE 5

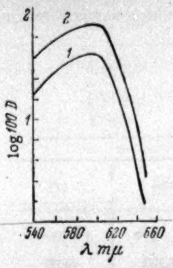
Electrical Conductivity of Nitrobenzene Solutions of Hydriodides of Malachite Green and Crystal Violet

c (moles/liter)	(VII)		(VIII)	
	$\varkappa \cdot 10^5$	λ	$\varkappa \cdot 10^5$	λ
$1 \cdot 10^{-2}$	20.6	20.6	19.3	19.3
$2 \cdot 10^{-3}$	4.68	23.4	4.42	22.1
$4 \cdot 10^{-4}$	1.01	25.2	0.94	23.6
$8 \cdot 10^{-5}$	0.208	26	0.196	24.5
$1.6 \cdot 10^{-5}$	—	—	0.04	25.0

Tris-(p-dimethylaminophenyl)-carbinol (II), methyl ether of tris-(p-dimethylaminophenyl)-carbinol (IV) and α-anilino-tris-(p-dimethylaminophenyl)-methane (VI). The electrical conductivity of nitrobenzene solutions of these compounds was systematically determined over a period of 30 days from the moment of preparation of the solutions. Results are presented in Table 6.

The absorption spectra of a nitrobenzene solution of compound (II), plotted immediately after preparation and after the lapse of 15 days, are shown in the diagram.

The optical densities of nitrobenzene solutions of compounds (II), (IV), (VI) and (VIII) with a concentration of $1.6 \cdot 10^{-5}$ molar were identical when measured on the 30th day after preparation. After they had been kept for 30 days, the electrical conductivity started to fall and the color started to change in the case of nitrobenzene solutions whose concentrations were $1 \cdot 10^{-2}$, $2 \cdot 10^{-3}$, and $4 \cdot 10^{-3}$ molar. At the same time the electrical conductivity and color of nitrobenzene solutions with concentrations of $8 \cdot 10^{-5}$ and $1.6 \cdot 10^{-5}$ molar remained constant.



Absorption spectra of a nitrobenzene solution of tris-(p-dimethylaminophenyl)-carbinol. 1) immediately after dissolution, 2) 15 days later.

Bis-(p-dimethylaminophenyl)-phenylcarbinol (I), methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol (III), α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane (V). Nitrobenzene solution with concentrations of $2 \cdot 10^{-3}$ molar and lower were prepared by successive dilution at intervals of 15 days. Electrical conductivities were measured systematically after 30 days.

Data obtained after 1 hour and on the 30th day after preparation of the solutions are presented in Table 7.

Measurements carried out after several months showed that the electrical conductivity of these solutions no longer changes. At the same time their absorption spectra corresponded to the absorption spectrum of a nitrobenzene solution of Malachite Green hydriodide.

TABLE 6

Electrical Conductivity of Nitrobenzene Solutions of Derivatives of Crystal Violet

c (moles/liter)	Duration (days)	(II)		(IV)		(VI)	
		$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ
$1 \cdot 10^{-2}$	1	0.91	0.09	3.35	0.33	4.43	0.44
	2	1.8	0.18	7.25	0.72		
	4	2.77	0.28	10.01	1.0		
	6	3.45	0.35	11.3	1.13		
	8	3.90	0.39	12.2	1.22		
	13	4.95	0.5	12.6	1.26		
	30	8.1	0.8	13.2	1.32	13.32	1.32
$2 \cdot 10^{-3}$	1	0.46	0.23	2.43	1.21	2.55	0.25
	2	1.7	0.85	3.8	1.9		
	4	2.53	1.26	6.1	3.05		
	6	3.25	1.63	7.2	3.6		
	8	3.7	1.85	7.5	3.75		
	13	4.34	2.17	7.8	3.9		
	30	5.36	2.68	12	6		
$4 \cdot 10^{-4}$	1	0.133	0.334	1.8	4.5		
	2	1.51	3.78	2.7	6.75	2.27	5.68
	4	2.25	5.6	3.8	9.5		
	6	2.94	7.35	4.3	10.7		
	8	3.20	8	4.8	12.0		
	13	3.42	8.55	5.3	13.2		
	30	4.54	11.3	7.7	17.5	5.78	14.4
$8 \cdot 10^{-5}$	1	0.03	0.37	1.55	19.3		
	2	0.92	11.5	1.77	22.1	0.54	6.75
	4	1.57	19.6	1.8	22.5		
	6	1.78	22.2	1.8	22.5		
	8	1.79	22.3	1.8	22.5		
	13	1.79	22.3	1.8	22.5		
	30	1.79	22.3	1.8	22.5	1.57	19.6
$1.6 \cdot 10^{-5}$	1				12.5		
	2	0.166	10.44	0.200			
	4	0.35	21.8	0.368	23		
	6	0.364	22.8	0.368	23		
	8	0.364	22.8	0.368	23		
	13	0.364	22.8	0.368	23		
	30	0.364	22.8	0.368	23		

TABLE 7

Electrical Conductivity of Nitrobenzene Solutions of Derivatives of Malachite Green

c (moles/liter)	Duration: A-1 hour B-30 days	(I)		(III)		(V)	
		$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ	$\varkappa \cdot 10^6$	λ
10^{-2}	A	1.54	0.15	1.23	0.12	2.23	0.22
	B	3.2	0.32	2.7	0.27	7.5	0.75
$2 \cdot 10^{-3}$	A	0.64	0.32	0.68	0.34	2.2	1.1
	B	1.62	0.81	1.44	0.72	3.5	1.8
$4 \cdot 10^{-4}$	A	0.39	0.97	0.42	1.05	1.0	2.5
	B	0.8	2.0	0.89	2.23	1.76	4.4
$1.6 \cdot 10^{-4}$	A	0.25	1.56	0.3	1.88	—	—
	B	0.785	4.9	0.94	5.85	—	—
$8 \cdot 10^{-5}$	A	—	—	—	—	0.43	5.35
	B	—	—	—	—	1.01	12.0

TABLE 8

Optical Density of Nitrobenzene Solutions

Compound	(VII)	(I)	(III)	(V)
c (moles/liter)	$3.2 \cdot 10^{-5}$	$1.6 \cdot 10^{-4}$	$1.6 \cdot 10^{-4}$	$8 \cdot 10^{-5}$
D	1.15	1.21	1.43	1.65

Optical densities for a wave-length of 600 mμ of some nitrobenzene solutions on the 30th day after their preparation are given in Table 8. The layer thickness of the investigated solutions was 4.94 mm.

SUMMARY

1. Iodides of Malachite Green and Crystal Violet behave in nitrobenzene solution like strong electrolytes. On dilution the electrical conductivity changes nearly proportionally to the degree of dilution, and equilibrium is established practically instantaneously.

2. The progressive dissociation of tris-(p-dimethylaminophenyl)-carbinol, methyl ether of tris-(p-dimethylaminophenyl)-carbinol, α-anilino-tris-(p-dimethylaminophenyl)-methane, bis-(p-dimethylaminophenyl)-phenylcarbinol, methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol, and α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane increases with the dilution.

3. The degree of dissociation of the above compounds in nitrobenzene solutions was determined at various dilutions. It was found that compounds of the Malachite Green group are less dissociated than the analogous compounds of the Crystal Violet group.

The limiting equivalent electrical conductivities of cations of Malachite Green and Crystal Violet and of OH', OCH_3' and NHC_6H_5' anions were found in nitrobenzene solutions.

5. Dissociation constants and isobaric potentials in nitrobenzene solutions were calculated for the iodides of Crystal Violet and Malachite Green, bis-(p-dimethylaminophenyl)-phenylcarbinol, methyl ether of bis-(p-dimethylaminophenyl)-phenylcarbinol and α-anilino-bis-(p-dimethylaminophenyl)-phenylmethane.

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Received December 18, 1956

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*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS ON CYCLIC ARYLAZO-β-DIKETONES

I. CONDENSATION OF 1,3-INDANDIOL WITH DIAZO COMPOUNDS

Z. Iu. Gudrinietse and G. Ia. Vanag

Compounds containing an active methylene group easily interact with diazo compounds [1, 2]. In continuation of our investigations on cyclic β-diketones, we were interested in their products of interaction with diazo compounds.

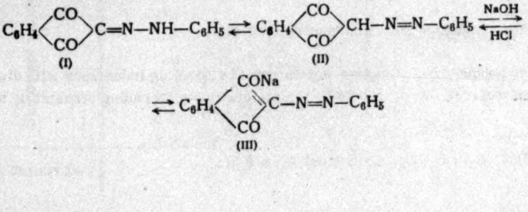
As far back as 1893, Wislicenus and Reitzenstein [3] reacted phenyldiazonium chloride with 1,3-indandione and obtained the β-phenylhydrazone of triketohydrindene (indantrione). Indandione was later condensed with diazotized p-nitroaniline, benzidine, p-toluidine and β-naphthylamine [4]. According to the patent literature [5-7] some indandione azo dyes can be successfully employed for dyeing of fabrics. Derivatives of phenylazoindandione find application in color photography [8]. In our opinion, theoretical and practical importance may be attached to a closer study of these compounds.

In our experiments we coupled 1,3-indandione with various diazotized amines and their derivatives at a pH of 2 to 10. The reaction goes with the highest speed in an alkaline medium, rather more slowly in a neutral medium, and most slowly in an acid medium. Coupling of indandione with diazonium salts in an acid medium is unknown; in fact the literature reports that cyclic β-diketones react only in an alkaline medium, although other compounds containing an active methylene group also react in an acid medium [9, 12].

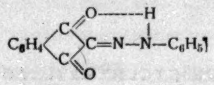
Products of coupling of indandione with diazo compounds (arylazoindandiones) are yellow to dark-red crystalline substances. They are very poorly soluble in water, ether, chloroform, carbon tetrachloride, gasoline, benzene, toluene and xylene, more soluble in glacial acetic acid, dioxane, acetone and alcohols (the solubility increases with increasing molecular weight of the alcohols), and relatively easily soluble in esters (ethyl acetate, benzyl acetate, methyl and ethyl benzoates). A list of the products that we obtained by coupling indandione with diazotized aromatic amines is given in the Table.

We made a more detailed study of 2-phenylazo-1,3-indandione. The name of this compound may not correspond to its structure, for according to the literature [3] it has the structure of a phenylhydrazone. We still adhere to the opinion that phenylazoindandione exists in two tautomeric forms (I, II) which are in equilibrium; depending upon the conditions, it reacts in the hydrazone (I) or azo (II) form.

Formula (II) is supported by the fact that phenylazoindandione dissolves in caustic alkali and is also slightly soluble in sodium carbonate when heated; it forms enolates (III), acidification of which leads to separation of the original phenylazoindandione (II).



Formula (II) is also supported by the inability of phenylazoindandione to cleave into indandione and phenylhydrazone either by treatment with alkalies or acids. Feofilaktov [10] points out that he also failed to hydrolyze butyrolactone phenylhydrazone. It is possible that the hydrazone form (I) contains a hydrogen bond which renders this form (IV) resistant to hydrolytic agents.



(IV)

Bromination of phenylazoindandione gives p-bromophenylazoindandione, which is also obtained on coupling indandione with diazotized p-bromoaniline. Sulfonation of phenylazoindandione gives p-sulfophenylazoindandione, which is also obtained by coupling of indandione with diazotized sulfanilic acid. It has good solubility in water and is isolated as the sodium salt. It imparts a bright-yellow color to wool and natural silk.

Nitration of phenylazoindandione gave p-nitrophenylazoindandione, which is identical with the product from indandione and diazotized p-nitroaniline. It is photosensitive and changes in color from yellow to greenish-brown.

The corresponding carbonyl group derivatives are formed by phenylazoindandione with phenylhydrazine, hydrazine and hydroxylamine. Reduction of phenylazoindandione gives various products (depending on the reaction conditions) whose examination is in progress.

EXPERIMENTAL

2-Phenylazo-1,3-indandione (I, II). 6.6 g of aniline in 18 ml of concentrated hydrochloric acid, diluted with 36 ml of water, was diazotized with 5.8 g of sodium nitrite. With constant stirring, the diazotized solution was run into a cooled solution of 10.3 g of indandione in sodium hydroxide solution. The mixed solution should have a pH of 7-9; more alkali can be added if needed. The liquid is left in a freezing mixture with constant stirring for 1.5-2 hr. and then acidified and suction-filtered. The product is crystallized from methanol or ethanol or their mixtures with glacial acetic acid, or from methyl or ethyl benzoate or benzyl acetate. The purest product and the highest yields are obtained from methanol or ethanol (10 g of crude product is dissolved with boiling in 700 ml of ethanol). The yield of 2-phenylazo-1,3-indandione is 12 g (68%); orange needles; m. p. 192-193° (the literature reports 190°). Insoluble in water and ether, poorly soluble in acetone, benzene and its homologs, better soluble in glacial acetic acid, alcohols and esters.

Found %: N 11.32. $C_{15}H_{10}O_2N_2$. Calculated %: N 11.20.

Other arylazoindandiones are similarly obtained by diazotization of other aromatic amines and coupling with indandione (see Table).

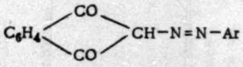
p-Bromophenylazoindandione. Bromine was added to 2.5 g of phenylazoindandione in 30 ml of glacial acetic acid and the mass was held at room temperature for 12-14 hours. The orange, crystalline precipitate was recrystallized from benzene. Yield 2.4 g (73%), m. p. 245°. Bromine is not split off on boiling with alkali.

Found %: N 8.53. $C_{15}H_9O_2N_2Br$. Calculated %: N 8.51.

The same p-bromophenylazoindandione was obtained by coupling indandione with diazotized p-bromoaniline in an alkaline medium. M. p. 243-245°; a mixture with the preceding preparation melts without depression.

Found %: N 8.85. $C_{15}H_9O_2N_2Br$. Calculated %: N 8.51.

2-Arylazo-1,3-indandiones



$C_6H_4{<}(CO)_2{>}CH-N=N-Ar$

Preparation No.	Diazotized amine	Ar	Recrystallized from	Melting point	Color	Empirical formula	Nitrogen content (%)	
							found	calc.
1	Aniline	C_6H_5	Ethanol	192—193°	Orange	$C_{15}H_{10}O_2N_2$	11.32	11.20
2	o-Nitroaniline	$o-C_6H_4NO_2$	Glacial acetic acid	290—292	Yellow	$C_{15}H_9O_4N_3$	14.37	14.23
3	m-Nitroaniline	$m-C_6H_4NO_2$	Dioxane	301—303	Yellow	$C_{15}H_9O_4N_3$	14.01	14.23
4	p-Nitroaniline	$p-C_6H_4NO_2$		311—313	Brownish	$C_{15}H_9O_4N_3$	14.48	14.23
5	p-Bromoaniline	$p-C_6H_4Br$	Benzene	243—245	Yellow	$C_{15}H_9O_2N_2Br$	8.85	8.51
6	o-Aminophenol	$o-C_6H_4OH$	Alcohol	250—252	Brownish	$C_{15}H_{10}O_3N_2$	10.56	10.52
7	m-Aminophenol	$m-C_6H_4OH$	Alcohol	273—274	Brown	$C_{15}H_{10}O_3N_2$	10.70	10.52
8	p-Aminophenol	$o-C_6H_4OH$	Alcohol	248—249	Red-brown	$C_{15}H_{10}O_3N_2$	10.65	10.52
9	o-Toluidine	$o-C_6H_4CH_3$	Alcohol	193—195	Orange	$C_{16}H_{12}O_2N_2$	10.81	
10	m-Toluidine	$p-C_6H_4CH_3$	Alcohol	185	Red	$C_{16}H_{12}O_2N_2$	10.68	10.60
11	p-Toluidine	$m-C_6H_4CH_3$	Alcohol	203	Brownish	$C_{16}H_{12}O_2N_2$	10.60	10.60
12	α-Naphthylamine	$\alpha-C_{10}H_7$	Benzyl acetate	232	Red	$C_{19}H_{12}O_2N_2$	9.47	9.33
13	β-Naphthylamine	$\beta-C_{10}H_7$	Benzyl acetate	242	Orange	$C_{19}H_{12}O_2N_2$	9.63	9.33
14	p-Aminoazobenzene	$p-C_6H_4-N=N-C_6H_4$	Pyridine	273—274	Red	$C_{21}H_{14}O_2N_4$	15.36	15.81
15	Anthranilic acid	$o-C_6H_4COOH$	Alcohol	—	Brownish	$C_{16}H_{10}O_4N_2$	8.81	9.52
16	m-Aminobenzoic acid	$m-C_6H_4COOH$	Alcohol	—	Yellow	$C_{16}H_{10}O_4N_2$	9.36	9.52
17	p-Aminobenzoic acid	$p-C_6H_4COOH$	Alcohol	—	Brownish	$C_{16}H_{10}O_4N_2$	—	—
18	Sulfanilic acid	$p-C_6H_4SO_3H$	Water (sodium salt)	—	Yellow	$C_{15}H_9O_5N_2SNa$	7.52	7.98

Sodium p-(indandionylazo)-benzenesulfonate. 0.5 g of phenylazoindandione and 5 ml of concentrated sulfuric acid were heated for 10-15 min. at 60°. The red solution turned yellow after dilution with water. The solution was saturated with sodium chloride. The sodium salt of indandionylazo-p-benzenesulfonic acid came down. Soluble in water and alcohol. It was purified by crystallization from water. In aqueous or acetic acid solution it colors wool and natural silk bright-yellow. The same product was obtained by coupling indandione with diazotized sulfanilic acid.

Found %: N 7.52, 7.45; Na 6.31. $C_{15}H_9O_5N_2SNa$. Calculated %: N 7.90; Na 6.51.

p-Nitrophenylazoindandione. 0.5 g of phenylazoindandione, 3 ml of glacial acetic acid and 3 ml of concentrated nitric acid were heated to 60-70°. The phenylazoindandione dissolved but a yellow precipitate came down at once. Crystallization from glacial acetic acid gave 0.2 g of yellow, finely crystalline p-nitrophenylazoindandione. M. p. 273°. Insoluble in water and ether, poorly soluble in alcohol and aromatic hydrocarbons; readily soluble in pyridine.

Found %: N 13.80, 14.63. $C_{15}H_9O_4N_3$. Calculated %: N 14.23.

The same p-nitrophenylazoindandione was prepared by coupling indandione with diazotized p-nitroaniline.

Phenylazoindandione monoxime. Five g of phenylazoindandione, 2.1 g of hydroxylamine hydrochloride and 100 ml of ethanol were boiled on a water bath for 1.5-2 hrs. The orange, finely crystalline precipitate was crystallized from dioxane. Yield of phenylazoindandione monoxime 5.2 g (98%). Yellow needles, m. p. 256-257°; m. p. 264-265° after crystallization from benzyl acetate.

Found %: N 15.78. $C_{15}H_{11}O_2N_3$. Calculated %: N 15.85.

Phenylazoindandione monophenylhydrazone. 1.25 g of phenylazoindandione, 2.16 g of phenylhydrazine and 70 ml of ethanol were boiled. The liquid turned red. Red crystals came down after 20 minutes. The mass was boiled for another 15 minutes. Crystallization from glacial acetic acid gave matted crystals with m. p. 241°.

Found %: N 16.92. $C_{21}H_{16}ON_4$. Calculated %: N 16.47.

Phenylazoindandione azine. 1.25 g of phenylazoindandione, 2.6 g of hydrazine sulfate, 1.64 g of anhydrous sodium acetate and 50 ml of ethanol were boiled for 2 hours. After cooling, the mass was poured into a 4-fold amount of water, and the precipitate was crystallized from ethanol. Dark-red needles of phenylazoindandione azine; m. p. 225-228°.

Found %: N 17.28. $C_{20}H_{20}O_2N_6$. Calculated %: N 16.93.

SUMMARY

1. Optimum conditions were established for the preparation of 2-phenylazo-1,3-indandione, a series of other 2-arylazo-1,3-indandiones were also synthesized.

2. A series of derivatives of 2-phenylazo-1,3-indandione were prepared: p-bromophenylazoindandione, p-nitrophenylazoindandione, p-sulfophenylazoindandione, phenylazoindandione monoxime, phenylazoindandione phenylhydrazone and azine.

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Received December 24, 1956

INVESTIGATIONS ON IMIDAZOLE DERIVATIVES

XVIII. THE PROBLEM OF THE NITRATION OF 5-METHYLBENZIMIDAZOLE*

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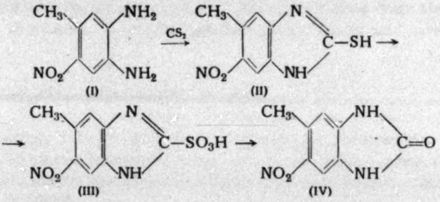
In a study of the chemical properties of derivatives of benzimidazole, we needed to prepare 5-methyl-6-nitrobenzimidazolone (IV) with precisely known location of the substituents. In this connection we carried out partial reduction of 2,4-dinitro-5-methylaniline. We obtained, however, a mixture of products from which it was fairly difficult to isolate the individual amines. Fusion of the mixture with urea leads to a still more impure product.

For the synthesis of substance (IV), we therefore decided to use an indirect route. Treatment of a mixture of the amines with carbon disulfide in a medium of alcoholic potassium hydroxide gave 5-methyl-6-nitro-2-mercaptobenzimidazole (II) which was very easily oxidized by permanganate in an alkaline medium to give the sulfoacid (III) which was hydrolyzed by hydrochloric acid to our required benzimidazolone derivative (IV).



For the purpose of identification of the starting 1,2-diamino-4-methyl-5-nitrobenzene (I), we decided to prepare from it the 2,5-dimethyl-6-nitrobenzimidazole (XI) previously described by Niementowski [1, 2]. On heating a mixture of the products of partial reduction of 2,4-dinitro-5-methylaniline with acetic anhydride, we obtained a substance that was found to be identical with the product of nitration of 2,5-dimethylbenzimidazole by Niementowski's method [1, 2].

By boiling our mixture of products of partial reduction of 2,4-dinitro-5-methylaniline with formic acid, we obtained a 65% yield of a substance melting at 197° and corresponding in empirical composition with methylnitrobenzimidazole. This compound must of course be 5-methyl-6-nitrobenzimidazole (X).

A melting point of 241° is given, however, in a paper by O. Fischer and W. Hess [3] for a product of the same structure synthesized by nitration of 5-methylbenzimidazole (V). Such a large difference in the melting points of the two preparations prompted us to repeat the experiments of O. Fischer and W. Hess [3] on the nitration of 5-methylbenzimidazole.

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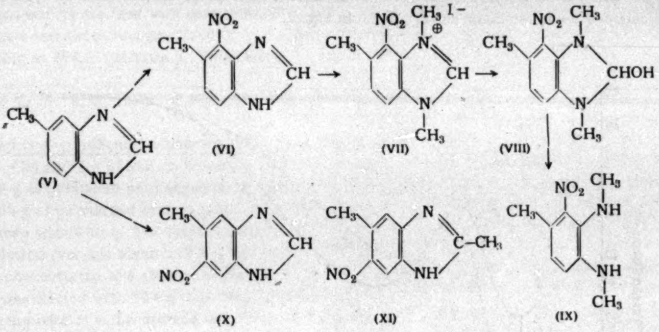
*Preceding communication: J. Gen. Chem. 27, 684 (1957).

On carrying out this reaction in concentrated sulfuric acid with theoretical quantity of nitric acid, we obtained a 75-80% yield of a product melting gradually at 180-220°. After 2 crystallizations from alcohol, we isolated a substance relatively sparingly soluble in alcohol and melting at 240°. The mother liquors from the purification yielded a compound very easily soluble in alcohol, identical with the 5-methyl-6-nitrobenzimidazole (X) that we had synthesized with m. p. 197°. The product with m. p. 240° also had the empirical composition of a methylnitrobenzimidazole and could only be the 5-methyl-4-nitro isomer (VI) since the third possible structural isomer – 5-methyl-7-nitrobenzimidazole – that we synthesized was very unlikely to be formed in the present case and had m. p. 289.5°.

O. Fischer and W. Hess based their assignment of the structure of the product with m. p. 241° on the transformation of this compound into di-(methylamino)-nitromethylbenzene with m. p. 194° by exhaustive methylation with methyl iodide and opening of the dihydroimidazole ring with alkali. They synthesized the same product by a similar route from 2,5-dimethyl-6-nitrobenzimidazole* obtained by them according to Niementowski's method [1, 2].

We also repeated this part of the work of Fischer and Hess [3]. From the substance with m. p. 240°, to which (as noted below) we must assign the structure of 5-methyl-4-nitrobenzimidazole (VI), we obtained the methoiodide of 1,5-dimethyl-4-nitrobenzimidazole (VII) with m. p. 212°, and from the latter we prepared 1,3,5-trimethyl-4-nitro-2-hydroxydihydrobenzimidazole (VIII) with m. p. 169°; finally, from the latter we obtained 1,2-di-(methylamino)-3-nitro-4-methylbenzene (IX) which melted at 30-31° and distilled without decomposition at 140° (3 mm). In the paper under comparison the respective melting points were 238, 150 and 194°.

It must be assumed that when they nitrated 5-methylbenzimidazole, Fischer and Hess did not observe the formation of two reaction products and performed all the transformations described above with their mixture; their end product was therefore evidently a mixture of ortho-diamines, of which 1,2-di-(methylamino)-3-nitro-4-methylbenzene, as we showed, is very low-melting and is distinguished by high solubility in organic solvents. It could be isolated with facility by recrystallization, and this circumstance enabled the authors in question to isolate 1,2-di-(methylamino)-4-methyl-5-nitrobenzene with m. p. 194° according to their data.



Having established that nitration of 5-methylbenzimidazole gives two isomeric nitro products, we attempted to evaluate their ratio. With this objective [4] we plotted the ultraviolet absorption spectra in ethanol of 5-methyl-6-nitrobenzimidazole (X) and 5-methyl-4-nitrobenzimidazole (VI), as well as of their mixture prepared in 75-80% yield by nitration (Fig. 1). **

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* An error evidently crept into the paper of Fischer and Hess [3]. The authors write that for 2,5-dimethyl-6-nitrobenzimidazole "in agreement with Niementowski m. p. 210° was found," whereas an m. p. of 201° is both by Niementowski [1] and by Maron and Salzberg [2] who repeated the work.

** The spectra were plotted with a Russian SF-4 spectrophotometer using quartz cells with a layer thickness of 1 cm (ethyl alcohol) and 0.5 cm (hydrochloric acid) at concentrations of respectively 3.9-3.6 · 10^{-5} and 6.9 · 10^{-5} mole/liter.

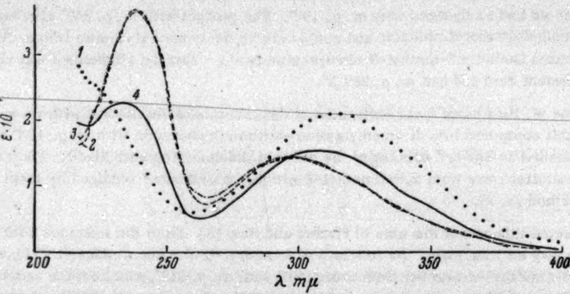

Fig. 1. Ultraviolet absorption spectra in ethyl alcohol. 1) 5-methyl-4-nitrobenzimidazole; 2) 5-methyl-6-nitrobenzimidazole; 3) 5-methyl-6-nitrobenzimidazole isolated from products of nitration of 5-methylbenzimidazole; 4) mixture of products of nitration of 5-methylbenzimidazole.

The mixture of isomers absorbed less intensively in the wavelength ranges of 220-230 mμ and 257-296 mμ than each of the components separately. Calculation on this basis gave a negative percentage content of isomers in the mixture and did not permit of any trustworthy calculations at other wavelengths. Reaction in solution of two amphoteric substances with different basicities was evidently involved [5]. This prompted us to study the absorption spectra of the investigated compounds in an acid medium whose pH was so low that hydrolysis of the salts was completely suppressed. As the solvent we selected 0.5% solution of hydrochloric acid, and we obtained the transmission curves plotted in Fig. 2.

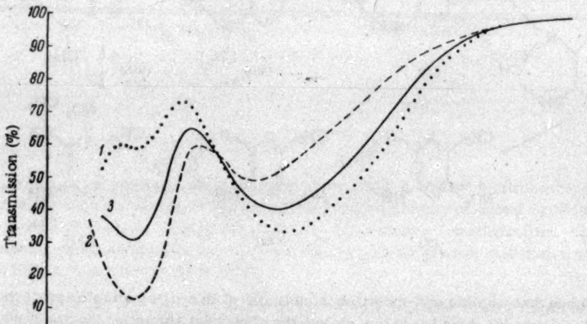

Fig. 2. Ultraviolet absorption spectra in 0.5% aqueous hydrochloric acid. 1) 5-methyl-4-nitrobenzimidazole; 2) 5-methyl-6-nitrobenzimidazole; 3) mixture of products of nitration of 5-methylbenzimidazole.

Wavelength (mμ)	5-Methyl-6-nitrobenzimidazole (%)	5-Methyl-4-nitrobenzimidazole (%)
232	42.7	57.3
290	43.6	56.4
300	43.2	56.8
Mean	43.1	56.9

Results of the calculations carried out for appropriate points [4] are presented in the Table.

Consequently, the nitration of 5-methylbenzimidazole gives a mixture of 4- and 6-nitro derivatives in the ratio of 5.7 : 4.3.

EXPERIMENTAL

Reduction of 2,4-dinitro-5-methylaniline. 23.7 g of 2,4-dinitro-5-methylaniline [6], 250 ml of ethyl alcohol, 50 ml of pyridine and 100 ml of concentrated aqueous ammonia were put into a flask fitted with a stirrer, a reflux condenser and a gas-leading tube extending to the bottom of the flask. With intensive stirring, a strong stream of hydrogen sulfide was passed through until the precipitate had completely dissolved (30-40 minutes). The heater was then removed and hydrogen sulfide was passed through for a further 20 minutes. The reaction mass was evaporated to dryness in vacuo and the dry residue was treated with three portions of a boiling mixture each comprising 90 ml of water and 10 ml of conc. hydrochloric acid. The extracts obtained were combined and heated with active carbon; after filtration from carbon and impurities, the liquid was cooled. Neutralization of the strongly colored solution with ammonia brought down dark-red crystals which weighed 12 g after drying and did not melt sharply at 126-129°.

5-Methyl-6-nitro-2-mercaptobenzimidazole (II). 6.4 g of diamine with m. p. 126-129°, 5 ml of hydrogen sulfide, 65 ml of alcohol and 4.2 g of potassium hydroxide were heated for 3 hours on a water bath in a flask connected with a reflux condenser. Seven ml of glacial acetic acid was then added and the solution was evaporated to dryness in vacuo. The dry residue was treated with 200 ml of boiling aqueous 2.5% solution of sodium hydroxide with addition of a few drops of aqueous sodium bisulfite solution. Treatment with active carbon scarcely decolorized the solution but facilitated filtration of the alkali-insoluble impurities. The cold mother liquor was neutralized with concentrated hydrochloric acid until neutral to Congo. After filtration, the precipitate was twice recrystallized from alcohol. An amorphous, easily electrified powder with a yellow color, melting at 284.5° (decomp.). Yield 3.5 g.

Found %: S 15.29, 15.02. $C_8H_7N_3O_2S$. Calculated %: S 15.33.

5-Methyl-6-nitrobenzimidazolone (IV). To a solution of 3.5 g of 5-methyl-6-nitro-2-mercaptobenzimidazole (II) and 1 g of sodium hydroxide in 25 ml of water was added (with stirring) a cold saturated solution of 2.65 g of potassium permanganate in water at such a rate that the temperature did not rise above 35°. Another 2.65 g of pulverized permanganate was then added, after which the manganese dioxide was filtered off and washed with water. The small excess of permanganate in the filtrate was removed with sodium bisulfite, the solution (volume about 100 ml) was neutralized with concentrated hydrochloric acid until acid to Congo and concentrated to a volume of 30 ml. A yellowish precipitate appeared during the evaporation. The suspension was diluted with 20 ml of concentrated hydrochloric acid and heated in sealed tubes for 3 hours at 120°. A strong odor of sulfur dioxide was detected when the tubes were opened. The precipitate was filtered, twice reprecipitated from alkali with acid and recrystallized from glacial acetic acid. Two g of 5-methyl-6-nitrobenzimidazolone (IV) was obtained in the form of faint-yellowish, fine needles with m. p. 325° (decomp.). The compound is sparingly soluble in organic solvents.

Found %: N 21.81, 21.71. $C_8H_7O_3N_3$. Calculated %: N 21.75.

5-Methyl-6-nitrobenzimidazole (X). A solution of 1 g of diamine with m. p. 126-129° in 10 ml of 100% formic acid was refluxed in a flask for 2 hours. 2.5 ml of concentrated hydrochloric acid was then added and the solution was evaporated to dryness in a dish on a water bath. The dry precipitate was dissolved in 20 ml of boiling water and treated with animal charcoal. After the charcoal had been filtered off, the cold mother liquor was acidified with excess of nitric acid. The precipitated nitrate of 5-methyl-6-nitrobenzimidazole was dissolved in 20 ml of boiling water and treated with animal charcoal; the resultant faintly colored solution was neutralized with ammonia. The precipitate was recrystallized 3 times from 50% aqueous alcohol. Slightly yellowish, very slender needles, easily soluble in alcohol, sparingly soluble in water; m. p. 197°. Yield 65%, reckoned on the diamine.

Found %: C 54.09, 54.01; H 4.03, 4.21. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

2,5-Dimethyl-6-nitrobenzimidazole (XI). A solution of 1 g of diamine with m. p. 126-129° in 10 ml of acetic anhydride was refluxed in a flask for 1 hour; 2.5 ml of concentrated hydrochloric acid was then added, and the solution was heated for another hour and evaporated to dryness in a dish on a water bath. The dry residue was dissolved in 20 ml of boiling water and treated with carbon; the filtrate was neutralized with ammonia. The precipitate was recrystallized 3 times from water and once from aqueous alcohol. The slightly yellowish powder, dried at 120°, melted at 200-201°. The product did not show a depression of melting point when mixed with the compound prepared by nitration of 2,5-dimethylbenzimidazole by Niementowski's method [1, 2].

5-Methyl-7-nitrobenzimidazole. 0.7 g of 1,2-diamino-3-nitro-5-methylbenzene [7] (m. p. 158°) and 6 ml of 100% formic acid were refluxed for 2 hours in a flask. Two ml of concentrated hydrochloric acid was then added, and the reaction mass was evaporated to dryness in a dish on a water bath. The dry residue was dissolved in 30 ml of boiling water and treated with carbon; the light-yellow solution was neutralized with ammonia. The precipitate was recrystallized twice from methanol. 5-Methyl-7-nitrobenzimidazole forms long, silky, nearly colorless needles with m. p. 289.5°, sparingly soluble in water and cold alcohol. Yield 70%.

Found %: C 54.33, 53.95; H 4.27, 4.01. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

5-Methylbenzimidazole (V). 5-Methylbenzimidazole was synthesized from 1,2-diamino-4-methylbenzene prepared, analogously to o-phenylenediamine [8], from 3-nitro-4-aminotoluene with the slight modification that the diamine was not isolated but the alcoholic solution containing the diamine was evaporated nearly to dryness in vacuo; the wet slurry was treated with a considerable excess of 85% formic acid and refluxed in a flask for 2 hours. Carbon was carefully added to the flask 20 minutes before the end of the reaction; the carbon was then filtered off and washed on the filter with a small quantity of warm water which was added to the reaction mass. The deeply colored solution was evaporated to dryness in a dish on a water bath; the dry residue was dissolved in water (800 ml for 0.5 mole of initial nitrotoluidine), and the cold solution was cautiously neutralized with ammonia with stirring. The precipitated product, which was badly contaminated at the start, was separated by filtration and centrifuged. The main bulk of 5-methylbenzimidazole came down in the form of a dark oil which was separated from the water and distilled in vacuo. 5-Methylbenzimidazole distilled without decomposition at 173° (3 mm) and set to a gummy, light-yellow mass. Yield 75% reckoned on the nitrotoluidine.

Nitration of 5-methylbenzimidazole. To a solution of 47 g of 5-methylbenzimidazole (V) in 185 ml of concentrated sulfuric acid was added 15 ml of nitric acid (d 1.5) at 0° with stirring. The reaction mass was stirred for 1 hour without cooling, the temperature rising to 20°. The yellow solution (about 900 ml) was poured on to ice; excess of nitric acid was then added. The precipitate was filtered off, well pressed,* and dissolved in the minimum quantity of boiling water; it was then precipitated from the hot solution with ammonia. Yield 75-80%. Crystallization from 1200 ml of alcohol gave 22.4 g of substance melting (after recrystallization) at 240°. The melting point of the 5-methyl-4-nitrobenzimidazole (VI) remained unchanged after further purification. The product is sparingly soluble in cold alcohol, almost insoluble in water.

Found %: C 53.96, 54.14; H 3.35, 3.60. $C_8H_7O_2N_3$. Calculated %: C 54.24; H 3.98.

Nearly complete evaporation of the alcoholic mother liquors after crystallization of the product described above led to separation of a substance melting at 167-187°.** Numerous recrystallizations from a small volume of alcohol enabled separation of a very small quantity of substance with m. p. 196°, easily soluble in alcohol. Judging by the absorption spectrum (Fig. 1), the crystal form, and the solubility, the compound is identical with 5-methyl-6-nitrobenzimidazole (X); a mixture with the latter melted at 196.5°.

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* A very small quantity of substance, which was not investigated, came out of the mother liquor on neutralization with ammonia.

** As in original – Publisher's note.

Methoiodide and methoperiodide of 1,5-dimethyl-4-nitrobenzimidazole. Four g of 5-methyl-4-nitrobenzimidazole (VI), 20 ml of methanol and 2.9 ml of methyl iodide were heated in a sealed tube for 5 hours at 140-150°. The precipitate was treated on the filter with three portions of 15 ml each of methanol and recrystallized from methanol. Rapid cooling resulted in deposition of light, thin, dark-red crystals of the periodide, melting at 114°. 0.6 g of the methoperiodide of 1,5-dimethyl-4-nitrobenzimidazole was obtained.

Found %: I 65.30, 64.98. $C_{10}H_{12}O_2N_3I_3$. Calculated %: I 64.87.

The methanol solution obtained on washing of the periodide was combined with the main filtrate and diluted with twice the volume of ether. The precipitate of methoiodide consisted of heavy, light-yellow needles with m. p. 212° (from alcohol). 3.5 g of 1,5-dimethyl-4-nitrobenzimidazole methoiodide (VII) was obtained.

Found %: C 36.19; H 3.07; I 38.32, 38.07. $C_{10}H_{12}O_2N_3I$. Calculated %: C 36.05; H 3.63; I 38.10.

1,3,5-Trimethyl-4-nitro-2-hydroxydihydrobenzimidazole (VIII). 4.5 g of 1,4-dimethyl-4-nitrobenzimidazole (VII) was dissolved in 50 ml of water, and an excess of 20% sodium hydroxide solution was added to the solution. A red oil separated out at once and rapidly crystallized and turned yellow. The precipitate was filtered off and recrystallized from aqueous alcohol containing active carbon. 2.3 g of a bright-yellow finely crystalline powder was obtained; m. p. 169°.

Found %: C 53.63, 53.55; H 5.87, 6.03. $C_{10}H_{13}O_3N_3$. Calculated %: C 53.80; H 5.87.

The same carbinol can be obtained by dropwise addition of an excess of aqueous bisulfite solution to a warm methanol solution or suspension of the periodide, slight dilution of the faintly yellowish solution with water, and precipitation of the product with alkali.

1,2-Di-(methylamino)-3-nitro-4-methylbenzene (IX). A mixture of 3.5 g of the above-described carbinol (VIII), 50 ml of water and 20 g of sodium hydroxide was distilled in steam until a red oil ceased to distill over (volume of liquid about 1 liter). The distillate was extracted with 4 portions of 30 ml each of chloroform, and the chloroform extracts were combined, washed with 40 ml of water and evaporated. The residue was distilled in vacuo: 1,2-di-(methylamino)-3-nitro-4-methylbenzene (IX) came over at 140° (3 mm). A fairly mobile liquid with a red color, rapidly crystallizing in the cold to light-red crystals melting at 30-31°. The product dissolves very easily in organic solvents and sparingly in water. Yield 2 g.

Found %: C 55.68, 55.40; H 6.69, 6.67. $C_9H_{13}O_2N_3$. Calculated %: C 55.32; H 6.72.

SUMMARY

1. Nitration of 5-methylbenzimidazole gives the 4- and 6-mononitro derivatives in the ratio of 5.7 : 4.3.

2. It was established that the product with m. p. 240° is 5-methyl-4-nitrobenzimidazole and not the 6-nitro derivative as claimed by O. Fischer and W. Hess.

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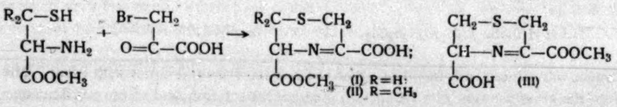
Leningrad Lensovet Institute of Technology Received December 18, 1956

THE CONDENSATION OF METHYL ESTERS OF α-AMINO-β-MERCAPTOCARBOXYLIC ACIDS WITH BROMOPYRUVIC ACID

I. T. Strukov

Condensation of methyl esters of L-cysteine and DL-penicillamine with bromopyruvic acid in a chloroform medium and in presence of triethylamine gave yellow crystalline substances (I) and (II) containing one free and one esterified carboxyl group. Judging by the analysis, they are derivatives of the 5,6-dihydrothiazine series whose double bond is evidently (in view of the course of the synthesis) in the 3,4-position.



Conclusive proof of the structure of these compounds has not yet been obtained since the possibility of migration of the double bond into the 2,3-position is not excluded.

Compounds (I) and (II) readily lose the carboxyl group on heating above 100°.

Condensation of cysteine hydrochloride with methyl bromopyruvate gave cystine hydrochloride and 5,6-dihydro-3-carbomethoxy-$\Delta^{3,4}$-thiazin-5-carboxylic acid (III).

The bromine in methyl bromopyruvate evidently possesses a positive charge and is capable of oxidizing sulfide groups.

EXPERIMENTAL

5,6-Dihydro-5-carbomethoxy-$\Delta^{3,4}$-thiazin-3-carboxylic acid. Into a 50 ml round-bottomed flask were placed 3 g of the hydrochloride of the methyl ester of L-cysteine, 2.9 g of bromopyruvic acid [1] and 30 ml of anhydrous chloroform; 7 ml of triethylamine was then added gradually with stirring and cooling. The solid material went into solution and the latter gradually acquired an orange-yellow color. The following day, the reaction mass was washed with 5 ml of water and 10 ml of 2 N hydrochloric acid; compound (I) was then extracted with 25 ml of 5% sodium bicarbonate solution. Treatment with active carbon at room temperature and careful acidification with concentrated hydrochloric acid led to isolation of 1.3 g of yellow prisms. The product was purified by conversion to the sodium salt and recrystallized from a small quantity of chloroform; m. p. 115° (decomp.). The compound dissolves in methyl and ethyl alcohol, acetone, chloroform and ethyl acetate; it is poorly soluble in water.

Found %: C 41.97, 41.88; H 4.71, 4.59; S 14.97. $C_7H_{11}O_4NS$. Calculated %: C 41.39; H 4.46; S 15.75.

The compound gives off carbon dioxide on melting.

5,6-Dihydro-6,6-dimethyl-5-carbomethoxy-$\Delta^{3,4}$-thiazin-3-carboxylic acid (II). To 3 g of the hydrochloride of the methyl ester of DL-penicillamine [2] were added 2.55 g of bromopyruvic acid and 30 ml of chloroform; 6.6 ml of triethylamine was then added gradually with stirring and cooling to 0°. The reaction mass gradually turned orange-yellow. Compound (II) was isolated as described above. It was purified by reprecipitation from the sodium salt. Light-yellow prisms. Yield 2.4 g (70%); m. p. 132-133° (decomp.). Soluble in the same solvents.

Found %: C 46.76; H 6.03; N 6.15; S 14.43; CH_3O 13.18. $C_9H_{13}O_4NS$. Calculated %: C 46.75; H 5.67; N 6.05; S 13.79; CH_3O 13.37.

Methyl bromopyruvate. The literature method [3] involves rapid addition of bromine to methyl pyruvate. This can lead to sudden liberation of hydrobromic acid and ejection of the reaction mass. In our procedure the methyl pyruvate was first treated with dry hydrogen chloride.

After dry hydrogen chloride had been passed through 20 g of methyl pyruvate for one minute, 32 g of bromine was gradually added from a dropping funnel. Bromination proceeded quietly and quickly. At the conclusion of the reaction, the light-yellow oil was heated in vacuo (15-20 mm) at 30-50° with the objective of eliminating hydrogen bromide; it was finally distilled at 6-7 mm and 84-87°. Yield 25.9 g (73%).

5,6-Dihydro-3-carbomethoxy-$\Delta^{3,4}$-thiazin-5-carboxylic acid. 0.8 g of cysteine hydrochloride, 1 g of methyl bromopyruvate and 3 ml of anhydrous dioxane were left at room temperature in a sealed tube for 3 days. The precipitate was filtered and recrystallized twice from a mixture of methanol and acetone. The white crystals of cystine hydrochloride melted at 187-188° (decomp.).

Found %: C 23.64; H 4.38. $C_6H_{14}O_4N_2S_2Cl_2$. Calculated %: C 23.00; H 4.50.

The mother liquor was diluted with 25 ml of water and extracted several times with ether. The compound was extracted from the ether solution with 5% sodium bicarbonate solution, and after acidification with sulfuric acid it was again extracted with ether. The ethereal solution was dried with magnesium sulfate and the ether was distilled off to leave a volume of 10 ml; cooling of the latter for several days led to separation of yellow crystals with m. p. 143-145° (decomp.).

Found %: C 41.26, 41.49; H 4.20, 4.49; N 6.63; CH_3O 14.75. $C_7H_9O_4NS$. Calculated %: C 41.44; H 4.46; N 6.89; CH_3O 15.27.

SUMMARY

A number of derivatives of 5,6-dihydro-$\Delta^{3,4}$-thiazin-3,5-dicarboxylic acids were prepared.

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Received December 19, 1956

INVESTIGATIONS ON CONJUGATED SYSTEMS

LXXXII. INFRARED SPECTRA OF VINYLACETYLENIC AND DIENIC ETHERS

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In previous communications we characterized the infrared spectra of some vinylacetylenic hydrocarbons and alcohols (the $C\equiv C-C=C$ conjugated system), as well as of acetylenic aldehydes and ketones (the $C\equiv C-C=O$ conjugated system) [1-3]. Continuing the study of the relation between structure, physical properties and reactivity, we have investigated the infrared spectra of some vinylacetylenic and dienic ethers with the general formulas: $R-C\equiv C-COR=CH_2$ and $R-CH=CH-COR=CH_2$.

The spectra of very few enolic ethers have hitherto been prepared [4]. We found no data in the literature for the spectra of ethers with conjugated multiple bonds.

Results of our measurements allow us to draw the following conclusions.

In the region of about 3300 cm^{-1} only an ether with a terminal acetylenic grouping absorbs intensively. The same phenomenon was also observed in the spectra of vinylacetylenic hydrocarbons and alcohols [1, 2]. In the spectra of acetylenic ketones, absorption of medium intensity was observed in this region also for compounds containing an acetylenic grouping in the middle of the chain [3].

In the region of valence CH vibrations (3150-2800 cm^{-1}) all of the ethers have 5 to 6 similar frequencies (in the various homologs). At least three of these belong to valence CH vibrations in alkyl radicals, possibly with superposition of other frequencies (for vinylacetylenic ethers: 2979, 2907-2924 and 2833 cm^{-1}; for dienic ethers: 2994, 2924 and 2809 cm^{-1}).* The 2870-2880 cm^{-1} appears in the spectra of compounds containing ethyl or larger radicals. Higher frequencies (3140 and 3020-3040 cm^{-1}) are associated with the presence of the CH_2 group. A frequency higher than 3100 cm^{-1} appears in the spectra of many compounds containing this group; it usually has a low intensity, however.

In the region of planar deformation CH vibrations, the spectra of vinylacetylenic ethers have not been closely characterized. There are usually 3-4 bands with values of frequencies differing little between the homologs. The band at 1450 cm^{-1} probably consists of 2 or 3 undifferentiated bands. In the spectra of dienic ethers these bands are resolved and a previously noted regularity is observed: the $CH_2=$ and $-CH_2-$ groups are associated respectively with absorption at 1414 and 1475 cm^{-1} [1].

Nonplanar deformation CH vibrations in the $CH_2=C$ grouping are represented in the spectra of vinylacetylenic ethers by an extremely characteristic band at 890 cm^{-1}. A dienic ether with a vinyl group absorbs at 923 and 985 cm^{-1}. The $-CH=CH-$ grouping corresponds to absorption at 960 cm^{-1}. These regularities are observed in the spectra of the most diverse unsaturated compounds [6, 7].

The triple bond of 3-methoxybuten-3-yne corresponds to a frequency of 2137 cm^{-1} in the spectrum, i.e., higher than in vinylacetylenic hydrocarbons and analogous structure (2114 cm^{-1}) [1]. In the spectra of other ethers with the structure of disubstituted acetylenes, the triple bond likewise corresponds to a higher frequency than in the spectra of hydrocarbons. The intensity of the frequency in question is higher than in the spectra of hydrocarbons and lower than in the spectra of acetylenic aldehydes and ketones.

Absorption bands corresponding to the double bond do not appreciably differ in the spectra of vinylacetylenic ethers from the same bands in the spectra of hydrocarbons in respect of position and intensity.

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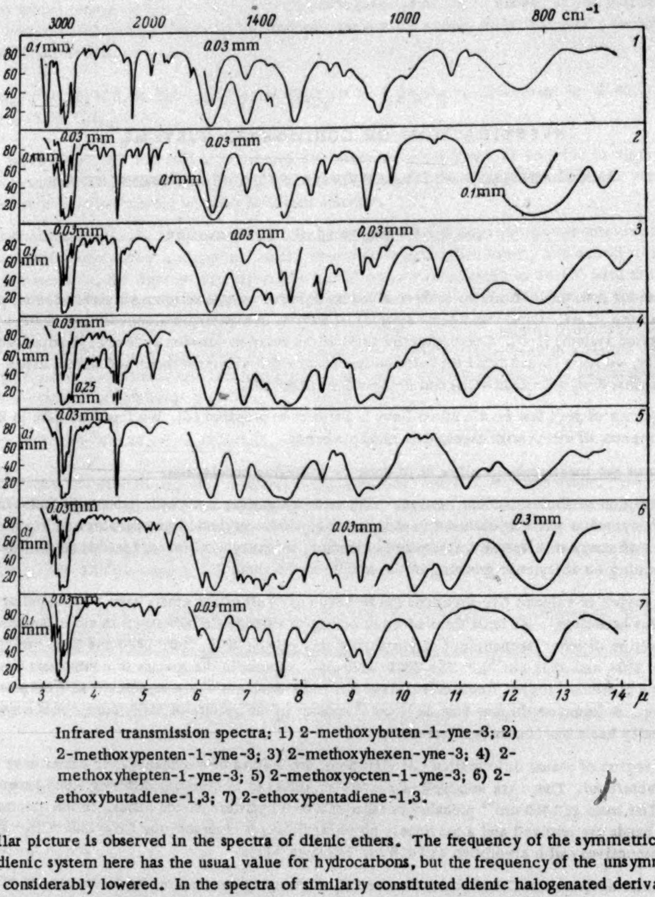
*The same frequencies appeared in the spectra of dimethyl ether and CH_3OH [5].



Infrared transmission spectra: 1) 2-methoxybuten-1-yne-3; 2) 2-methoxypenten-1-yne-3; 3) 2-methoxyhexen-yne-3; 4) 2-methoxyhepten-1-yne-3; 5) 2-methoxyocten-1-yne-3; 6) 2-ethoxybutadiene-1,3; 7) 2-ethoxypentadiene-1,3.

A similar picture is observed in the spectra of dienic ethers. The frequency of the symmetrical vibrations of the dienic system here has the usual value for hydrocarbons, but the frequency of the unsymmetrical vibrations is considerably lowered. In the spectra of similarly constituted dienic halogenated derivatives a marked lowering of both frequencies in comparison with the values in hydrocarbons is observed [9]. Consequently, a halogen atom more strongly deforms the dienic system than an alkoxy group.

This observation may be correlated with the susceptibility to polymerization of dienic ethers and halogenated derivatives. It is well-known that 2-ethoxybutadiene polymerizes 2000 times slower than chloroprene and only 3 times faster than isoprene [8].

The ether groups of dienic and vinylacetylenic ethers differ in reactivities; dienic ethers very much more easily undergo hydrolysis. In this connection it is of interest to compare the ν_{O-C} frequencies in the spectra of these two series of compounds. This is not yet possible, however, due to difficulties in plotting of the frequencies in the region where bands resulting from vibrations of the ether group can be expected. In the spectra that we investigated, these vibrations are presumably associated with bands in the 1150-1200 cm^{-1} region and possibly also in the region of approximately 1000 cm^{-1}.

$HC \equiv C-C(OCH_3)=CH_2$	$CH_3-C \equiv C-C(OCH_3)=CH_2$	$C_2H_5-C \equiv C-C(OCH_3)=CH_2$	$C_3H_7-C \equiv C-C(OCH_3)=CH_2$	$C_4H_9-C \equiv C-C(OCH_3)=CH_2$	$CH_2=CH-C(OC_2H_5)=CH_2$	$CH_3-CH=CH-C(OC_2H_5)=CH_2$
3300 (s)	—	—	—	—	—	—
3145 (w)	3140 (m)	3140 (m)	3140 (m)	3140 (w)	3140 (s)	3140 (m)
3025 (s)	3021 (s)	—	3021*(s)	3021*(s)	3044*(s)	3040 (s)
2979 (s)	2979 (s)	2979 (s)	2979 (s)	2979 (s)	2994 (s)	2994 (s)
2907*(s)	2915*(s)	2933 (s)	2941*(s)	2950*(s)	2924 (s)	2924 (s)
—	—	2874*(s)	2874 (s)	2874 (s)	2882*(s)	2882*(s)
2833 (s)	2833 (s)	2833 (s)	2833 (s)	—	2809 (m)	—
2725 (vw)	2725 (w)	2725 (w)	2725 (w)	2725 (w)	2747 (s)	2725*(s)
2646 (w)	2660 (vw)	2618 (w)	2660 (w)	2660 (w)	2618 (vw)	2604 (vw)
2591 (vw)	2577 (w)	2577 (vw)	2584 (w)	2584 (w)	2558 (vw)	—
2513 (w)	—	—	2532 (vw)	—	—	—
2475 (vw)	2475 (w)	2475 (w)	2481 (w)	2481 (vw)	2469 (vw)	2463 (vw)
2415 (w)	—	2415 (vw)	—	—	—	—
2392*(w)	2387 (w)	2387 (w)	2387*(w)	2387 (w)	2392 (vw)	2387 (vw)
—	—	—	2315*(w)	—	2299 (vw)	2299 (vw)
—	**2268** (s)	**2268** (s)	**2262** (s)	**2262** (s)	—	—
2218 (w)	2218 (w)	2188 (w)	—	—	2232 (vw)	—
2137 (s)	2134 (w)	2151 (w)	2110 (w)	2151 (vw)	2155 (vw)	—
2—	2066 (w)	2058 (vw)	—	—	2096 (vw)	2083 (vw)
1984 (m)	1984 (m)	1984 (w)	1961 (w)	1976 (w)	2000 (w)	2012 (w
—	1961 (w)	1953 (w)	—	—	1969 (w)	—
—	1930 (w)	1930 (w)	—	—	1923 (w)	1923 (w)
1855 (vw)	—	—	—	—	—	—
1821 (vw)	—	—	—	—	1835 (m)	1835 (vw)
1718 (vw)	—	—	—	—	1721*(m)	—
1603 (s)	**1603** (s)	**1603** (s)	**1603** (s)	**1608** (s)	**1645** (s)	**1664** (s)
—	—	—	—	—	**1575** (s)	**1575** (s)
—	—	—	—	—	1475 (s)	1475*(m)
1453 (s)	1453 (s)	1453 (s)	1456 (s)	1456 (s)	1449 (s)	1449 (s)
—	—	—	—	—	1414 (s)	—
1368 (s)	1392 (s)	1374 (s)	1377*(s)	1377*(s)	1374 (s)	1381 (s)
—	—	1328 (s)	1330*(s)	1330*(s)	1357*(s)	—
—	—	—	—	—	1309 (s)	1309 (s)
1277 (s)	1292 (s)	1289 (s)	1292 (s)	1292 (s)	1241 (s)	1244 (s)
1195 (s)	1192 (s)	1196 (s)	1196 (s)	1193 (s)	1202 (m)	1180 (m)
1155 (m)	1156 (m)	1153 (m)	1153 (m)	1153 (m)	1159*(s)	1156 (m)
—	—	—	—	—	1120 (s)	1107 (s)
1078*(s)	1086 (s)	1092 (s)	1096 (s)	1096 (s)	1092*(s)	1075 (s)
—	—	—	—	1060 (s)	—	—
1058 (s)	1031 (s)	1040 (s)	1049 (s)	1040*(s)	1029*(s)	—
—	—	—	1026*(m)	—	—	—
1005*(s)	—	—	1005*(s)	994 (w)	—	—
—	978 (w)	988 (w)	979*(w)	975 (w)	985 (s)	963 (s)
—	956 (m)	943 (m)	—	963 (w)	954*(s)	—
916 (s)	—	—	—	—	923 (s)	911*(m)
894*(m)	889 (s)	882 (s)	895 (s)	895 (s)	—	—
—	—	—	—	864 (m)	—	—
826 (s)	811 (s)	824 (s)	817 (s)	818 (s)	800*(s)	826*(s)
737 (m)	733 (m)	—	741 (m)	741 (m)	758*(m)	790 (s)
701 (m)	—	718 (m)	—	728 (m)	—	—

• Frequencies marked with a star are superposed on other frequencies. Frequencies of a conjugated system of multiple bonds are in bold type.

• • (s) – strong, (w) – weak, (vw) – very weak, (m) – medium.

EXPERIMENTAL

The work was carried out with the substances previously described [10-12]. More accurate constants were obtained for some of the ethers. We give them in the following order: b. p. (at 20 mm), d_4^{20}, n_D^{20}.

$CH_3-C\equiv C-C(OCH_3)=CH_2$: 39°, 0.8832, 1.4690.

$C_2H_5-C\equiv C-C(OCH_3)=CH_2$: 52.5 — 53°, 0.8724, 1.4675.

$C_3H_7-C\equiv C-C(OCH_3)=CH_2$: 67 — 67,5°, 0.8686, 1.4662.

$C_4H_9-C\equiv C-C(OCH_3)=CH_2$: 84—84.5°, 0.8657, 1.4660.

Infrared spectra were photographed with the IKS-2 apparatus. Working conditions are given in the preceding papers. The experimental data are presented in the Diagram and in the Table.

SUMMARY

1. Infrared spectra of a series of vinylacetylenic and 1,3-dienic ethers were investigated (2-methoxybuten-1-yne-3; 2-methoxypenten-1-yne-3; 2-methoxyhexen-1-yne-3; 2-methoxyhepten-1-yne-3; 2-methoxyocten-1-yne-3; 2-ethoxybutadiene-1,3; and 2-ethoxypentadiene-1,3).

2. Some regularities in the position and intensity of absorption bands corresponding to systems of multiple bonds were noted.

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Received December 30, 1956

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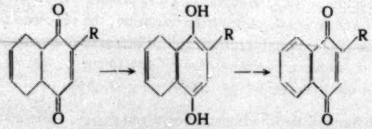
*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS ON QUINONES

XX. PREPARATION OF NAPHTHOQUINONES AND DIHYDROANTHRAQUINONES

A. N. Grinev and A. P. Terent'ev

Methods of synthesis of p-naphthoquinones based on oxidation of 1-amino-4-hydroxynaphthalenes [1, 2], 1,4-diaminonaphthalenes [3], naphthalene [4], 2-methylnaphthalene [5], etc. [6, 7] either lead to low yields of 1,4-naphthoquinones [3-7] or are inconvenient in practice [1, 2]. Condensation of p-benzoquinone and toluquinone with butadiene has also been utilized for the preparation of 1,4-naphthoquinone (VII) and 2-methyl-1,4-naphthoquinone (VIII).



(I) R=H (II) R=CH_3 (III) R=Cl

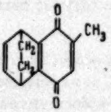
(IV) R=H (V) R=CH_3 (VI) R=Cl

(VII) R=H (VIII) R=CH_3 (IX) R=Cl

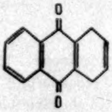
Although adducts of p-quinones with butadiene (I), (II) and (III) are obtained in yields close to the quantitative, complications arise through isomerization of the adducts to the substituted hydroquinones (IV), (V) and (VI). For example, the isomerization by hydrobromic acid of larger quantities of adducts than 5-10 g leads according to our observations to secondary reactions. We found that isomerization goes especially well on short-period heating of the adducts with acetic acid at the boil. We effected oxidation of hydroquinones (IV), (V) and (VI) to quinones (VII), (VIII) and (IX) with chromic acid. The preparation of adducts (I), (II) and (III), their isomerization and the oxidation of hydroquinones (IV), (V) and (VI) were realized without separation of intermediate compounds. 1,4-Naphthoquinone (VII) and 2-methyl-1,4-naphthoquinone (VIII) were obtained in 77-83% yield (calculated on the p-benzoquinone and toluquinone).

We previously synthesized p-quinones of the dihydronaphthalene series with the help of potassium bromate in an acid medium; this was found to be a very convenient oxidant [10]. The relatively poorly accessible dihydronaphthoquinones were obtained by this method in nearly quantitative yield.

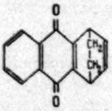
In the present work we oxidized hydroquinones with potassium bromate and obtained 5,8-endoethylene-5,8-dihydro-2-methyl-1,4-naphthoquinone (X), 1,4-dihydroanthraquinone (XI) and 1,4-endoethylene-1,4-dihydroanthraquinone (XII).



(X)



(XI)



(XII)

The reaction was conducted under conditions similar to those described in our preceding papers [10, 11].

EXPERIMENTAL*

1. 1,4-Naphthoquinone (VII). 600 ml of acetic acid in a thick-walled flask was saturated (ice-cooling) with 101 g of butadiene. To the resultant solution was added 145 g of p-benzoquinone. The reaction vessel was tightly closed and stood for 48 hours at room temperature. The adduct (I) was isomerized by refluxing of the reaction solution for 4 hours at the boiling point of acetic acid. The resultant hydroquinone (IV) solidified to a dense, white crystalline mass. One liter of acetic acid was added to the reaction mixture to dissolve the hydroquinone. An aqueous solution of chromic acid (prepared by dissolving 307 g of chromic oxide in 307 ml of water) was gradually added to the solution with stirring by a mechanical stirrer. The chromic acid solution was added at such a speed that the temperature of the reaction mixture did not exceed 70-75°. The mixture was then heated for an hour at 70-75°. The solution was cooled to room temperature and diluted with sevenfold volume of water. The 1,4-naphthoquinone (VII) was filtered off and dried. M. p. 124°, in agreement with the literature [4]. Yield 167 g (77%).

2. 2-Methyl-1,4-naphthoquinone (VIII). Adduct (II) was prepared from 30 g of toluquinone, 30 g of butadiene and 150 ml of acetic acid. After isomerization as described above, 200 ml of acetic acid was added to the reaction mixture. The hydroquinone (V) was oxidized with aqueous chromic acid prepared from 54 g of chromic oxide and 54 ml of water. All of the operations were performed as in Experiment 1. M. p. of 2-methyl-1,4-naphthoquinone (VIII) 104-105°. The literature [9] reports m. p. 104°. Yield 36.6 g (83.6%).

3. 2-Chloro-1,4-naphthoquinone (IX). Adduct (III) was prepared from 75 g of chloro-p-benzoquinone, 42 g of butadiene and 300 ml of acetic acid. After isomerization, the reaction solution was diluted with 500 ml of acetic acid. Hydroquinone (VI) was oxidized with chromic acid prepared from 119 g of chromic oxide and 119 ml of water. The operations were performed as in Experiment 1. M. p. of 2-chloro-1,4-naphthoquinone 117°, in agreement with the literature [12]. Yield 40 g (38.6%).

4. 2-Methyl-5,8-endoethylene-5,8-dihydronaphthohydroquinone. The adduct of toluquinone with cyclohexadiene with m. p. 88° (3.2 g), prepared by the known method [13], was dissolved in acetic acid and boiled for 4 hours (gentle boiling of the acetic acid). The resultant solution was diluted with water. An oily layer separated out and crystallized on cooling. 3 g of crystals of the hydroquinone was obtained. M. p. 175-176°; literature: m. p. 177° [13].

5. 2-Methyl-5,8-endoethylene-5,8-dihydro-1,4-naphthoquinone (X). To a solution of 3 g of 2-methyl-5,8-endoethylene-5,8-dihydroanthraquinone in 30 ml of dioxane was added a hot solution of 1.5 g of potassium bromate and 1.5 ml of 1 N sulfuric acid in 15 ml of water. The reaction mixture was heated for 2-3 minutes to form a transparent, yellow solution; this was cooled and diluted with 100 ml of water. Crystals of quinone (X) were collected and dried in a vacuum-desiccator over calcium chloride. M. p. 84-85°. Literature: m. p. 85-86° [13]. Yield 2.8 g.

6. 1,4-Dihydroanthrahydroquinone. The adduct of 1,4-naphthoquinone with butadiene with m. p. 104-105°, prepared by the literature method [14], was isomerized by heating with acetic acid as above. 1,4-Dihydroanthrahydroquinone came out of the acetic acid solution in the form of white crystals which very quickly darken in the air. Yield 3.5 g (from 4 g of adduct). M. p. 205-207° (from aqueous alcohol).

Found %: C 79.45, 79.32; H 5.34, 5.43. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

7. 1,4-Dihydroanthraquinone (XI). The experiment was performed with 3 g of 1,4-dihydroanthrahydroquinone, 1.5 g of potassium bromate, 30 ml of dioxane, 15 ml of water, and 1.5 ml of 1 N sulfuric acid. The procedure was the same as for Experiment 5. 2.6 g of the quinone (XI) was obtained with m. p. 210°. Literature: m. p. 208-210° [15].

8. 1,4-Dihydro-1,4-endoethyleneanthrahydroquinone. The adduct from 1,4-naphthoquinone and cyclohexadiene (m. p. 135°), obtained by the published procedure [15], was isomerized by heating with acetic acid as described above. 4.5 g of adduct gave 4 g of 1,4-dihydro-1,4-endoethyleneanthrahydroquinone. M. p. 200-202° (from aqueous alcohol).

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* Carried out with participation of V. K. Lomova.

Found %: C 80.93, 80.95; H 5.90, 5.63. $C_{16}H_{14}O_2$. Calculated %: C 80.64; H 5.92.

9. 1,4-Dihydro-1,4-endoethyleneanthraquinone (XII). The experiment was carried out with 3 g of 1,4-dihydro-1,4-endoethyleneanthrahydroquinone, 1.5 g of potassium bromate, 30 ml of dioxane, 15 ml of water and 1.5 ml of sulfuric acid. Procedure as above. Yield of the quinone (XII) 2.7 g. M. p. 176-178°. Literature: m. p. 180° [15].

SUMMARY

1. It was shown that isomerization of adducts of quinones with dienic hydrocarbons by heating in acetic-acid solutions leads smoothly to substituted hydroquinones.

2. A method was developed for the preparation of 1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone and 2-chloro-1,4-naphthoquinone; it involved reaction of p-benzoquinone, toluquinone and chloro-p-benzoquinone with butadiene without isolation of intermediate compounds.

3. Oxidation of the corresponding hydroquinones with potassium bromate in an acid medium by the previously developed procedure gave 2-methyl-5,8-dihydro-5,8-endoethylene-1,4-naphthoquinone, 1,4-dihydroanthraquinone and 1,4-dihydro-1,4-endoethyleneanthraquinone.

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Received December 28, 1956

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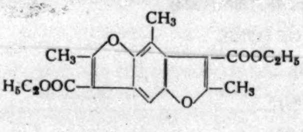
*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS ON QUINONES

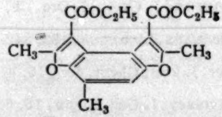
XXI. THE STRUCTURE OF SUBSTANCES PREPARED BY CONDENSATION OF TOLUQUINONE AND α-NAPHTHOQUINONE WITH ETHYL ACETOACETATE

A. N. Grinev and A. P. Terent'ev

Graebe and Levy [1], who investigated the reaction of toluquinone with ethyl acetoacetate, found that this reaction gives a mixture of two compounds with m. p. 173 and 122°. Due to the death of one of the authors, however, no further work was carried out in this field [1]. In one of our investigations we recently established that the compound with m. p. 120-122° is formed predominantly if the reaction is performed with rapid addition of toluquinone to a mixture of ethyl acetoacetate, zinc chloride and alcohol while heating [2]. Two possible structures can be advanced for this compound (I) and (II) :

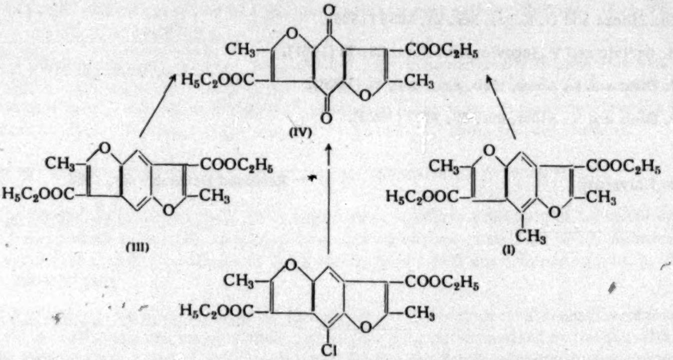


(I)



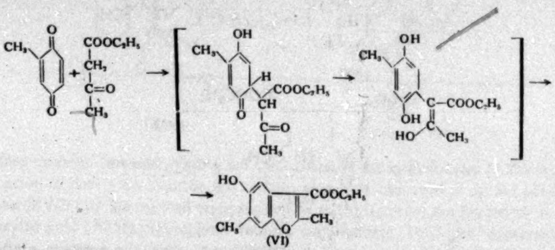
(II)

By oxidation with chromic acid of the diethyl ester of 2,6-dimethylbenzo-(1,2-b; 4,5-b')-difuran-3,7-dicarboxylic acid (III) we obtained the quinone (IV) of the benzodifuran series. According to our observations, quinone (IV) is obtained, in poor yield it is true, by oxidation of chlorine-substituted benzodifuran (V). Since the same compound is also formed by oxidation of the benzodifuran derivative resulting from condensation of toluquinone with ethyl acetoacetate, we can assume that this substance is the diethyl ester of 2,4,6-trimethylbenzo-(1, 2-b; 4,5-b')-difuran-3,7-dicarboxylic acid (I).

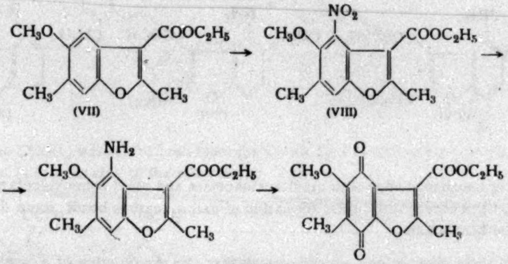


The structural formulas of compounds (III) and (V) are not in doubt [3-5].

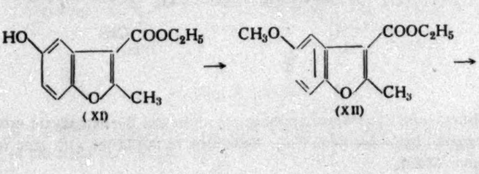
The ethyl ester of 2,6-dimethyl-5-hydroxybenzofuran-3-carboxylic acid (VI) with m. p. 173° is obtained in 43% yield by condensation of toluquinone with ethyl acetoacetate in an alcoholic solution of zinc chloride when the toluquinone is added very slowly.

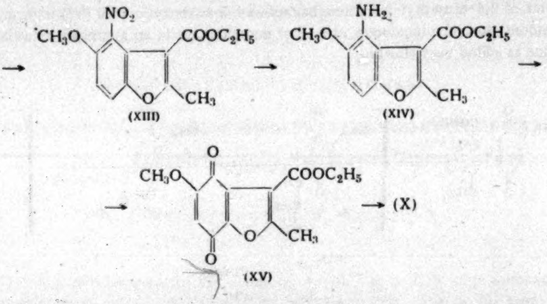

(VI)

Consequently, in this case the CH_3 group in the p-quinone nucleus directs the molecule of ethyl acetoacetate into the position opposite to the substituent, or (by analogy with the benzene series) into the para-position. The structure of the substituted benzofuran (VI) was confirmed by the following route:

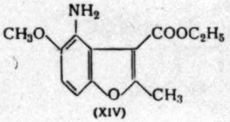

(VII) (VIII) (IX) (X)

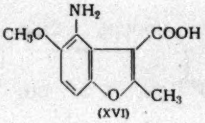
The ethyl ester of 2,6-dimethyl-5-methoxybenzofuran-3-carboxylic acid (VII) was prepared by methylation of (VI) with dimethyl sulfate. Nitration of (VII) with nitric acid (d 1.43) in acetic acid leads to the ethyl ester of 2,6-dimethyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (VIII); reduction of the latter over platinum catalyst gives the corresponding amino compound (IX). Compound (IX) is oxidized by potassium dichromate in a sulfuric acid medium to the ethyl ester of 2,6-dimethyl-5-methoxybenzofuranquinone-3-carboxylic acid (X), but in insignificant yield. We prepared the quinone (X) from the known [6] ethyl ester of 2-methyl-5-hydroxybenzofuran-3-carboxylic acid (XI) by a similar series of transformations.

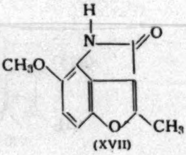

(XI) (XII)



The ethyl ester of 2-methyl-5-methoxybenzofuranquinone-3-carboxylic acid was methylated with lead tetraacetate by Fieser's procedure [7]. The structure of the ethyl ester of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XIV) was confirmed by cyclization (by heating) of the aminoacid (XVI), obtained by hydrolysis of the ester (XIV), to the amide (XVII).

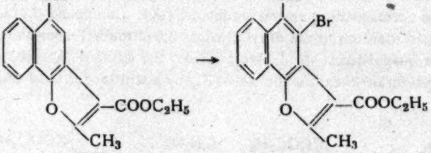

(XIV)


(XVI)

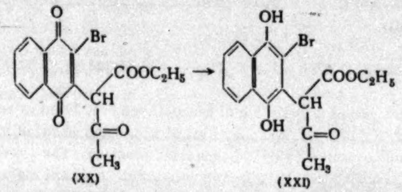

(XVII)

Condensation of p-benzoquinone with ethyl acetoacetate and ethyl benzoylacetate, as our investigations have shown [6, 8], proceeds with initial formation of carbon-carbon bonds, since the reaction leads to 5-hydroxy-substituted benzofurans.

On the basis of these observations, we can assume that also the reaction of α-naphthoquinone with ethyl acetoacetate, previously studied by us [9], leads to the ethyl ester of 2-methyl-5-hydroxy-α-naphthofuran-3-carboxylic acid (XVIII). With the objective of obtaining more definite proof of the structure of the α-naphthofuran (XVIII), we attempted to synthesize by reverse synthesis the ethyl ester of 2-methyl-4-bromo-5-hydroxy-α-naphthofuran-3-carboxylic acid (XIX) prepared from it.

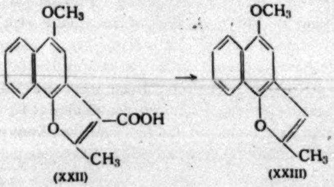


As the starting substance for the reverse synthesis we chose the 3-acetoacetic ester of 2-bromo-1,4-naphthoquinone (XX) prepared by Liebermann [10]. Reduction of the latter with zinc in acetic acid gave the corresponding hydroquinone (XXI).



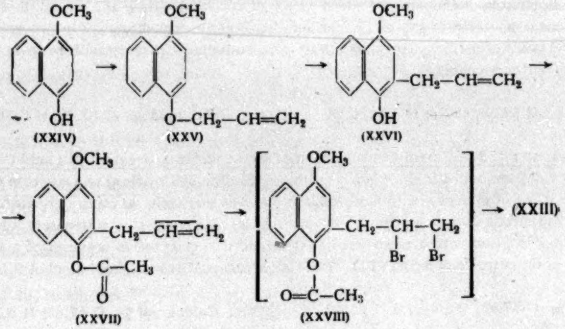
O
Br
COOC₂H₅
CH
O
C=O
CH₃
(XX)
OH
Br
COOC₂H₅
CH
OH
C=O
CH₃
(XXI)

Complications ensued, however, during the cyclization of the hydroquinone (XXI) to the naphthofuran (XIX) under the action of both zinc chloride and sulfuric acid. We then carried out the proof of the structure of the naphthofuran (XVIII) by the method once applied by us [6], namely: the 2-methyl-5-methoxy-α-naphthofuran-3-carboxylic acid (XXII) [9] prepared from the naphthofuran (XVIII) was converted by decarboxylation into 2-methyl-5-methoxy-α-naphthofuran (XXIII).



OCH₃
COOH
O
CH₃
(XXII)
OCH₃
O
CH₃
(XXIII)

The naphthofuran (XXIII) was synthesized from the known [11] 4-methoxy-1-hydroxynaphthalene (XXIV) by the Claisen reaction [12] according to the scheme:



OCH₃
OH
(XXIV)
OCH₃
O—CH₂—CH=CH₂
(XXV)
OCH₃
—CH₂—CH=CH₂
OH
(XXVI)
OCH₃
—CH₂—CH=CH₂
O—C—CH₃
O
(XXVII)
OCH₃
—CH₂—CH—CH₂
Br Br
O
O=C—CH₃
(XXVIII)
(XXIII)

EXPERIMENTAL

1. Diethyl ester of 2,6-dimethylbenzo-(1,2,-b;4,5-b')-difuroquinone-3,7-dicarboxylic acid (IV). a) To a solution of 10.2 g of benzodifuran (III) in 197 ml of acetic acid was added a solution of chromic acid

(prepared from 24.7 g of chromic oxide, 16 ml of water and 132 ml of 98% acetic acid) in the course of an hour with stirring and gentle boiling of the acetic acid. The reaction solution was diluted with double the volume of water. The crystals of the quinone (IV) were filtered, dried and twice recrystallized from acetic acid. Yield 6.5 g. The quinone (IV) has good solubility in acetic acid, dioxane and dichloroethane; m. p. 103-104° (from acetic acid).

Found %: C 59.93, 59.86; H 4.68, 4.72. $C_{18}H_{16}O_8$. Calculated %: C 60.00; H 4.48.

b) An experiment was performed with 3 g of benzodifuran (V), 70 ml of acetic acid, and a solution of chromic acid prepared from 8 g of chromic oxide, 4 ml of water, and 45 ml of 98% acetic acid. The reaction and isolation of the product were carried out as in experiment (a). The yield after recrystallization from acetic acid was 0.9 g; m. p. of (IV) 103-104° (from acetic acid). A mixed melting test with the quinone (IV) prepared in experiment (a) did not give a depression of melting point.

c) An experiment was run with 2.5 g of benzodifuran (I) and 60 ml of 98% acetic acid. The chromic acid solution was prepared from 7 g of chromic oxide, 4 ml of water and 35 ml of acetic acid (98%). Reaction and isolation of product were carried out as before. Yield of quinone (IV) 0.6 g; m. p. 103-104° (from acetic acid). A mixed melting test with the quinone (IV) obtained in experiment (a) did not give a depression of melting point.

2. Ethyl ester of 2,6-dimethyl-5-hydroxybenzofuran-3-carboxylic acid (VI). The experiment was performed in accordance with our procedure in a Soxhlet without a siphon [13]. 28 grams of zinc chloride was dissolved in 30 ml of anhydrous alcohol in the flask of the Soxhlet with heating. To the resultant solution were added 52 g of ethyl acetoacetate and 20 ml of absolute ether. 24 grams of toluquinone was placed in the thimble of the Soxhlet. The flask was heated on an air bath at 90-100° (thermometer in bath), and the Soxhlet discharged 15-17 drops per minute. The toluquinone was extracted from the thimble into the reaction flask for 15 hours, after which heating was carried out for 45 minutes at 95-100°. The crystals that deposited after cooling of the reaction liquid were collected and recrystallized from methanol and dichloroethane-acetone mixture (1 : 1). Yield of benzofuran (VI) 20 g, m. p. 173° (in agreement with the literature [1]).

Found %: C 67.02, 67.04; H 6.30, 6.18. $C_{13}H_{14}O_4$. Calculated %: C 66.65; H 6.02.

3. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuran-3-carboxylic acid (VII). 11.7 g of the hydroxybenzofuran (VI) was dissolved in 40 ml of dioxane. The solution was mixed with 50 ml of 2 N sodium hydroxide. To the suspension of phenate was added 12.6 g of dimethyl sulfate and the mixture was shaken for 35 minutes at room temperature. The transparent reaction solution was diluted with two volumes of water and cooled. The crystals of methoxybenzofuran (VII) were collected and recrystallized from alcohol. Yield 13 g, m. p. 123-124° (from alcohol).

Found %: C 67.80, 67.94; H 6.74, 6.78. $C_{14}H_{16}O_4$. Calculated %: C 67.73; H 6.50.

4. Ethyl ester of 2,6-dimethyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (VIII). 1.7 ml of nitric acid (d 1.43) was added in 15 minutes (with ice-cooling and stirring) to a solution of 3.4 g of benzofuran (VII) in 30 ml of glacial acetic acid; the mixture was then left at room temperature; the temperature rose to 25°. The mixture was heated at 37-40° for 1 hour. 2.5 volumes of water were added and the mass was cooled. A viscous layer separated; this was rubbed with a glass rod in presence of a little alcohol and gave crystals of the nitro compound (VIII). Yield after recrystallization from alcohol 2.9 g, m. p. 112-113°.

Found %: C 57.49, 57.60; H 5.32, 5.40. $C_{14}H_{15}O_6N$. Calculated %: C 57.33; H 5.16.

5. Ethyl ester of 2,6-dimethyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (IX). 1.5 g of nitro compound (VIII) was mixed with 30 ml of anhydrous alcohol in a glass hydrogenating vessel; 0.1 g of platinum oxide was added. The mixture was shaken in a hydrogen atmosphere for 7 hours. The catalyst and unreacted nitro compound were filtered off and washed on the filter with a little ether. The filtrates were evaporated in vacuo in the absence of air and the precipitate was dissolved in a little absolute ether. Gradual evaporation of the ether was accompanied by separation of crystals of amine (IX). Yield 0.6 g after recrystallization from a mixture of ligroine with alcohol; m. p. 106°.

Found %: C 63.76, 63.64; H 6.56, 6.60. $C_{14}H_{17}O_4N$. Calculated %: C 63.86; H 6.51.

6. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuroquinone-3-carboxylic acid (X). To a suspension of 1 g of amine (IX) in 35 ml of water were added (with cooling) 5 ml of conc. sulfuric acid and 0.6 g of pulverized potassium dichromate. The reaction mixture was left overnight at room temperature. An additional 0.6 g of potassium dichromate was then added and the mixture was left for 3 hours. The quinone was extracted from the precipitate and the aqueous layer with ether; the ethereal extracts were combined and dried with calcium chloride. Evaporation of the ether left 0.12 g of quinone (X) with m. p. 116-117° (from alcohol).

Found %: C 60.56, 60.64; H 4.77, 4.86. $C_{14}H_{14}O_6$. Calculated %: C 60.43; H 5.07.

7. Ethyl ester of 2-methyl-5- methoxybenzofuran-3-carboxylic acid (XII). Methylation of the hydroxybenzofuran (XI) was performed as above (experiment 3). Reaction components were 44 g of hydroxybenzofuran (XI), 200 ml of 2 N sodium hydroxide, 40 ml of dimethyl sulfate and 80 ml of dioxane. Yield of methoxybenzofuran (XII) 50 g; m. p. 46-47° (from alcohol).

Found %: C 66.63, 66.60; H 5.99, 5.90. $C_{13}H_{14}O_4$. Calculated %: C 66.65; H 6.02.

8. Ethyl ester of 2-methyl-4-nitro-5-methoxybenzofuran-3-carboxylic acid (XIII). The experiment was performed with 21 g of methoxybenzofuran (XII), 11.1 ml of nitric acid (d 1.43),150 ml of acetic acid. The nitric acid was added at 20° in the course of 30 minutes. The mass was held at 35-37° for 1 hour. The reaction liquid was diluted with three volumes of water and cooled; the precipitate was collected and recrystallized twice from a mixture of alcohol and dioxane (4:1). Yield of nitro compound (XIII) 17 g; m. p. 146-148°.

Found %: C 56.18, 56.14; H 4.60, 4.70. $C_{13}H_{13}O_6N$. Calculated %: C 55.91; H 4.70.

9. Ethyl ester of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XIV). Reduction of nitro compound (XIII) was effected as described above (experiment 5). The experiment was carried out with 8.4 g of nitro compound (XIII), 0.1 g of platinum oxide and 50 ml of anhydrous alcohol. The reaction period was 4 hours. Catalyst and unreacted nitro compound (XIII) were separated and the filtrate was worked up as before. 1.8 g of crystals of amine (XIV) was obtained by recrystallization from a mixture of ligroine and alcohol; m. p. 127-128°.

Found %: C 62.47, 62.44; H 6.29, 6.22. $C_{13}H_{15}O_4N$. Calculated %: C 62.64; H 6.07.

Treatment of amine (XIV) with hydrochloric acid in the usual manner gave the hydrochloride with m. p. above 180° (with decomp.).

Found %: C 54.53, 54.47; H 5.54, 5.60. $C_{13}H_{16}O_4NCl$. Calculated %: C 54.66; H 5.64.

10. Ethyl ester of 2-methyl-5-methoxybenzofuroquinone-3-carboxylic acid (XV). Oxidation of amine (XIV) to the quinone (XV) was effected as described above (experiment 6). Components were 3 g of amine (XIV), 3.6 g of potassium diochromatex and 15 ml of conc. sulfuric acid. Yield of quinone (XV) 0.35 g; m. p. 155-157° (from aqueous dioxane).

Found %: C 59.00, 58.88; H 4.60, 4.63. $C_{13}H_{12}O_6$. Calculated %: C 59.09; H 4.58.

11. Ethyl ester of 2,6-dimethyl-5-methoxybenzofuroquinone-3-carboxylic acid (X). Methylation of quinone (XV) with lead tetraacetate was effected by the known procedure [7]. 0.5 g of quinone (XV) was dissolved in 10 ml of glacial acetic acid, and 0.3 g of malonic acid and 2.5 g of lead tetraacetate were added. The reaction mixture was heated at 50-60° for an hour on a air bath. 2.5 g of lead tetraacetate was added and heating continued for 1.5 hours at 75°. The reaction mixture was poured into water, the precipitated quinone (X) was collected and recrystallized from alcohol. Yield of purified quinone 0.15 g; m. p. 116°. A mixed melting test with quinone (X) obtained in experiment 6 did not give a depression of melting point.

12. 2-Methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XVI). 0.1 g of sodium hydroxide was dissolved in 6 ml of alcohol, and 6 ml of ether and 0.5 g of amine (XIV) were added. The reaction mixture was refluxed in a small flask, shielded against contact with air by a Bunsen valve, for 1 hour at 60-80°. The reaction liquid was diluted with 3 volumes of water and acidified with dilute hydrochloric acid (litmus test). In the vicinity of the neutral point, the light-green acid (XVI) came down. Yield 0.38 g; m. p. >220° (decomp.) after recrystallization from a mixture of ethyl alcohol and ligroine (1 : 5).

Found %: C 59.65, 59.68; H 4.88, 4.92. $C_{11}H_{11}O_4N$. Calculated %: C 59.72; H 5.01.

13. Inner amide of 2-methyl-4-amino-5-methoxybenzofuran-3-carboxylic acid (XVII). 0.2 g of amino acid (XVI) was heated for 1 hour with 2 ml of quinoline at 180-220°; the cooled reaction solution was treated with dilute hydrochloric acid; the crystals of amide (XVII) were collected and recrystallized from nitrobenzene. Yield 0.1 g; m. p. 193-195°.

Found %: C 64.90, 64.85; H 4.60, 4.49. $C_{11}H_9O_3N$. Calculated %: C 65.02; H 4.46.

14. Ethyl ester of 2-methyl-4-bromo-5-hydroxy-2-naphthofuran-3-carboxylic acid (XIX). To a solution in 30 ml of dioxane of 3 g of the naphthofuran (XVIII), prepared by us previously [9], was added dioxane dibromide prepared by dissolving 0.17 g of bromine in 5 ml of dioxane. The resultant transparent, light-yellow solution was diluted with water and cooled. The crystals of bromoderivative (XIX) were collected and recrystallized from alcohol. Yield 3.6 g; m. p. 93-94°.

Found %: Br 22.75, 22.80. $C_{16}H_{13}O_4Br$. Calculated %: Br 22.92.

15. Bromonaphthohydroquinone-acetoacetic ester (XXI). 5 g of bromo-α-naphthoquinone-acetoacetic ester (XX) [10] was dissolved in acetic acid in the cold. To the solution was added zinc powder in small portions with gentle heating until the the solution had decolorized. The solution was separated from the deposit and diluted with water. The crystals were collected and recrystallized from alcohol. Yield of the hydroquinone (XXI) 3 g; m. p. 114-116°.

Found %: C 51.99, 52.15; H 4.09, 4.12. $C_{16}H_{15}O_5Br$. Calculated %: C 52.31; H 4.09.

16. 2-Methyl-5-methoxy-α-naphthofuran (XXIII). A mixture of 9.6 g of the methoxy acid (XXII) [9] and 5.6 g of calcium oxide was heated in a Wurtz flask over a bare flame; a syrupy oil distilled over; the latter was taken up in ether, dried with calcium chloride and distilled at reduced pressure. Yield of naphthofuran (XXIII) 4 g; b. p. 154-155° (1 mm).

Found %: C 79.29, 79.36; H 5.85, 5.88. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

The picrate of the naphthofuran, prepared in the usual manner, melted at 131-132° (from alcohol).

Found %: C 54.58, 54.49; H 3.44, 3.42. $C_{20}H_{15}O_9N_2$. Calculated %: C 54.43; H 3.43.

17. Allyl ether of 4-methoxy-1-naphthol (XXV). 28.6 g of 4-methoxy-1-naphthol (XXIV) [11], 35.5 ml of anhydrous acetone, 16.9 g of allyl bromide and 27.18 g of potassium carbonate were placed in a round-bottomed flask. The reaction mixture was heated on a water bath for 19 hours, then treated with water and extracted with ether. The ethereal extract was washed with 2 N sodium hydroxide and dried with calcium chloride. The viscous liquid product was distilled at reduced pressure. Yield of the allyl ether (XXV) 21 g, b. p. 140° (1 mm).

Found %: C 78.66, 78.73; H 6.76, 6.85. $C_{14}H_{14}O_2$. Calculated %: C 78.48; H 6.59.

18. 2-Allyl-4-methoxy-1-naphthol (XXVI). 14 grams of the allyl ether of 4-methoxy-1-naphthol (XXV) was heated at 240° on an oil bath in a vacuum of 22 mm for 1.5 hours; the 2-allyl-4-methoxy-1-naphthol (XXVI) was then distilled at reduced pressure. Yield 10.5 g; b. p. 155-156° (1 mm); m. p. 50° (from alcohol).

Found %: C 78.88, 78.96; H 6.71, 6.75. $C_{14}H_{14}O_2$. Calculated %: C 78.48; H 6.59.

19. 1-Acetoxy-2-allyl-4-methoxynaphthalene (XXVII). 7.68 g of 2-allyl-4-methoxy-1-naphthol (XXVI) was mixed with 8 ml of acetic anhydride, and a few drops of conc. sulfuric acid were added. The reaction mixture was heated for 1.5 hours on a water bath, cooled, and dissolved in ether. The ethereal solution was washed with dilute sodium hydroxide and dried with sodium sulfate. Compound (XXVII) was distilled at reduced pressure. Yield 6.5 g; b. p. 164-167° (1 mm); m. p. 91-92° (from alcohol).

Found %: C 75.19, 75.09; H 6.38, 6.33. $C_{16}H_{16}O_3$. Calculated %: C 74.98; H 6.29.

20. 2-Methyl-5-methoxy-α-naphthofuran (XXIII). 5.88 g of 1-acetoxy-2-allyl-5-methoxynaphthalene (XXVII) was dissolved in 6 ml of chloroform. To the cooled and stirred solution was added 1 ml of bromine in 8 ml of chloroform (dropwise). After bromination had been completed (evident from the decolorization of the solution), the chloroform was taken off in vacuo. The residual dibromo compound (XXVIII) was mixed with a saturated solution of 6 g of potassium hydroxide in methyl alcohol and heated for 31 hours on a water bath. The solution was separated from the potassium bromide, the alcohol was distilled off, and the resultant oil was taken up in ether and dried with calcium chloride. Yield of naphthofuran (XXIII) 1.4 g; b. p. 154-155° (1 mm). The picrate melted at 131°. A mixed melting test with 2-methyl-5-methoxy-α-naphthofuran (XXIII) from experiment 16 did not give a depression of melting point.

SUMMARY

1. The structure of the products of condensation of toluqinone and α-naphthoquinone with ethyl acetoacetate was confirmed.

2. When the reaction of toluquinone with ethyl acetoacetate is carried out slowly, the methyl group of toluquinone directs the molecule of ethyl acetoacetate into the para-position.

3. A number of substituted benzofurans, benzodifurans and naphthofurans were prepared.

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Received December 28, 1956

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*Original Russian pagination. See C. B. Translation.

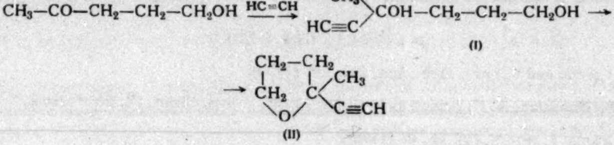
THE MECHANISM OF THE DEHYDRATION OF γ-GLYCOLS

V. STUDY OF THE PROPERTIES AND TRANSFORMATIONS OF THE ACETYLENIC γ-GLYCOL 3-METHYL-1-HEXYN-3,6-DIOL

T. A. Favorskaia and O. V. Sergievskaia

In preceding communications [1, 2] we showed that the alcohols 2-phenyl-2-penten-5-ol and 3-methyl-3-hexen-1-yne-6-ol, which contain a system of conjugated double bonds, do not isomerize to the corresponding tetrahydrofuran derivatives under the mild conditions that we employed for a series of β-ethylenic alcohols [3, 4]. Transformation of 2-phenyl-2-penten-5-ol into 2,2-methylphenyltetrahydrofuran required very much more drastic conditions, while the enynic alcohol completely resinified under these conditions.

Wishing to prepare 2,2-methylethynyltetrahydrofuran (II), which we required for further syntheses, we synthesized the acetylenic γ-glycol 3-methyl-1-hexyn-2,6-diol (I), in the expectation that, like other investigated γ-glycols [3, 4] it would be dehydrated to the tetrahydrofuran derivative on treatment with very dilute sulfuric acid.

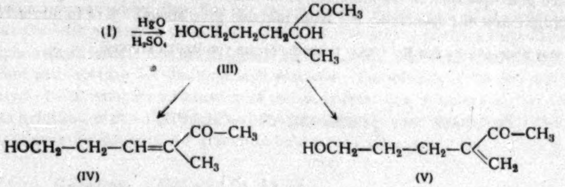


Condensation of acetopropyl alcohol with acetylene was effected by the method of A. E. Favorskii. The resultant glycol was an extremely unusual compound. Its most striking feature was that it did not react under ordinary conditions with ammoniacal silver oxide; a precipitate of silver derivative was formed only on heating of the reaction mixture nearly to the boil; the precipitate of silver derivative is poorly soluble in nitric acid; it formed a yellowish powder; it detonated when an attempt was made to weigh it for analysis.

On the other hand, on heating the glycol with potassium hydroxide solution, it broke down to acetopropyl alcohol and acetylene; the quantity of hydrogen taken up on hydrogenation over platinum black corresponded to the presence of a triple bond in the glycol molecule. Ozonization of the glycol yielded about 40% of formic acid; oxidation with potassium permanganate was unsuccessful, but oxidation with nitric acid (5 volumes of acid to 1 volume of water) gave acetone and acetic and levulinic acids. The glycol was hydrated in presence of Kucherov catalyst to the anticipated ketoglycol (III) in 69% yield. This was a crystalline substance which on standing with 2,4-dinitrophenylhydrazine solution gave a precipitate of the 2,4-dinitrophenylhydrazone; complete analysis of this compound revealed, however, that its composition corresponds not to a derivative of the ketoglycol but to a derivative of the unsaturated ketoalcohol; evidently on standing with a sulfuric acid solution of 2,4-dinitrophenylhydrazine the ketoglycol undergoes dehydration, and the resultant ketoalcohol reacts with the 2,4-dinitrophenylhydrazine. The ketoglycol itself does not form a 2,4-dinitrophenylhydrazone.

Hydration of the glycol gave a small quantity of low-boiling fraction which distilled over a fairly wide range; it yielded 2,4-dinitrophenylhydrazone whose composition corresponded to the derivative of the unsaturated ketoalcohol but which melted at a temperature different from that of the 2,4-dinitrophenylhydrazone described above. Consequently, treatment of the glycol with a sulfuric acid solution of mercuric oxide leads to partial dehydration of the ketoglycol with formation of some other unsaturated ketoalcohol.

Dehydration of the ketoglycol can proceed in two directions:



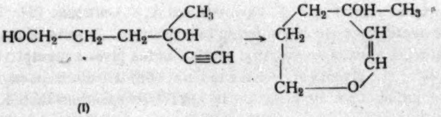
$$(I)\xrightarrow[H_2SO_4]{HgO} HOCH_2CH_2CH_2C(OH)(COCH_3)CH_3\ (III)$$

$$HOCH_2{-}CH_2{-}CH{=}C(CO{-}CH_3)CH_3\ (IV) \qquad HOCH_2{-}CH_2{-}CH_2{-}C({=}CH_2)CO{-}CH_3\ (V)$$

In order to establish which of the two ketoalcohols is formed when the ketoglycol is stood with a sulfuric acid solution of 2,4-dinitrophenylhydrazine, we stood the ketoglycol with a sulfuric acid solution of the same concentration but obtained no ketoalcohol at all; the ketoglycol was recovered unchanged; this signifies that 2,4-dinitrophenylhydrazine has some catalytic action, and in its absence the ketoglycol does not undergo dehydration.

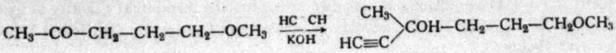
The presence of a carbonyl group in the molecule of the ketoglycol was confirmed by plotting of the ultraviolet absorption spectrum.

Consequently, all of the properties and transformations of the glycol, as well as the spectrographic data (infrared and Raman), compel us to assign the formula (I) to it; and explanation was still lacking, however, for the inability of the glycol to react with ammoniacal silver oxide at room temperature. It might be suggested that the glycol possesses another structure and acquires structure (I) under the influence of reactants or high temperature. It is well-known [3, 4] that the hydrogen of the primary alcoholic group in β-ethylenic alcohols easily migrates to the β-carbon atom to form tetrahydrofuran derivatives. We suspected that the hydrogen of the primary alcohol group of glycol (I) migrates to the δ-carbon atom with formation of an unstable seven-membered oxide ring which is readily cleaved under the influence of reagents.



(I)

We therefore decided to replace the primary hydroxyl of the glycol by a methoxy group and to thereby obtained a compound with a free acetylenic hydrogen. For this purpose it was necessary to prepare the methyl ether of acetopropyl alcohol and to condense it with acetylene. We were able to prepare this ether only by reacting acetopropyl alcohol with dimethyl sulfate, all of the other common methods of synthesis of ethers being unsuccessful in the present case. The prepared ether (VI) was condensed with acetylene in presence of pulverized potassium hydroxide.



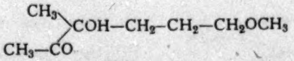
$$CH_3{-}CO{-}CH_2{-}CH_2{-}CH_2{-}OCH_3 \xrightarrow[KOH]{HC\ CH} (CH_3)(HC{\equiv}C)COH{-}CH_2{-}CH_2{-}CH_2OCH_3$$

(VI) (VII)

The behavior of ether (VII) towards ammoniacal silver oxide was entirely similar to that of glycol (I): the silver derivative only came down when the reaction mixture was heated. Consequently, the hypothesis of the transformation of the glycol into a cyclic compound by migration of the hydroxyl hydrogen to the δ-carbon atom proved to be untenable, and it was necessary to seek for another explanation of this unusual behavior of the glycol and its ether towards ammoniacal silver oxide solution. With this objective we made a close study of the properties of ether (VII).

The presence of a triple bond in the molecule of the ether was confirmed through the Raman spectrum, as well as by hydrogenation and ozonolysis; the latter reaction gave about 65% of formic acid.

The ether was hydrated by the Kucherov procedure; the resultant carbonyl



(VIII)

compound (VIII) corresponded in composition to the above formula, and the ultraviolet spectrum confirmed the presence of the carbonyl group; nevertheless, compound (VIII) did not react either with 2,4-dinitrophenylhydrazine or with semicarbazide. We may recollect that the ketoglycol (III), as such, also did not react with 2,4-dinitrophenylhydrazine, only the product of its dehydration (the unsaturated ketoalcohol) entering into reaction. On the other hand, it is well-known [2] that the product of dehydration of glycol (III) – the enynic alcohol 3-methyl-3-hexen-1-yn-6-ol – differs from the glycol in instantaneously reacting in the cold with ammoniacal silver oxide solution. The impression is created that in order for the acetylenic hydrogen and the carbonyl group in the compounds in question to manifest their inherent properties the neighboring tertiary hydroxyl group must be absent. However, all of the known acetylenic alcohols with the general formula RR'COH–C≡CH immediately give precipitates with the silver reagent [5-7], and the products of their hydration react with semicarbazide and 2,4-dinitrophenylhydrazine [8]. Whatever role is also played by the terminal hydroxyl and methoxyl groups present in one of the radicals, in their absence the reactions with the reagents in question proceed normally. The data obtained are certainly as yet insufficient for a conclusive explanation of the anomalous behavior of the glycol and its derivatives, and further investigations of this problem are necessary.

EXPERIMENTAL

Synthesis of 3-methyl-1-hexyn-3,6-diol (I). The γ-glycol was prepared by condensation of acetopropyl alcohol with acetylene in presence of pulverized potassium hydroxide under the conditions worked out for the synthesis of acetylenic glycols by A. E. Favorskii and A. S. Onitsenko [9]. The yield of glycol was 30-40% reckoned on the acetopropyl alcohol entering into reaction. In spite of many fractional distillations, the glycol always contained a trace of acetopropyl alcohol which gives a precipitate of 2,4-dinitrophenylhydrazone with m. p. 143°. The glycol only ceased to react with 2,4-dinitrophenylhydrazine after treatment with a freshly prepared solution of sodium bisulfite; its ultraviolet spectrum then demonstrated the absence of a carbonyl group.

B. p. 136.5° (17 mm), n_D^{20} 1.4718, d_4^{20} 1.0220, MR_D 35.06. $C_7H_{10}O_2$ ⫢. Calculated 35.57.

Found %: C 65.61; H 9.55; number of active H 1.94. M 145 (in dioxane). $C_7H_{10}O_2$. Calculated %: C 65.51; H 9.45; number of active H 2. M 128.

Hydrogenation of 3-methyl-1-hexyn-3,6-diol. 11.5 g of glycol was hydrogenated in anhydrous alcohol in presence of 1.2 g of platinum black. Ninety-two percent of the theoretical quantity of hydrogen was absorbed, calculated for the triple bond. The isolated product was fractionally distilled at 12 mm. The following fractions were obtained:

1st, 126-129°, 2 g, n_D^{20} 1.4540; 2nd, 129-130.5°, 8.5 g, n_D^{20} 1.4572, d_4^{20} 0.9607, MR_D 37.43; calcd. 37.57.

The constants found are in agreement with the literature data for 3-methylhexane-3,6-diol [10].

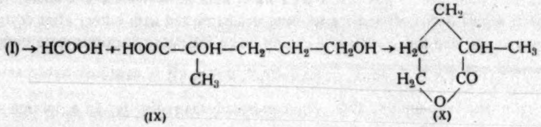
Decomposition of 3-methyl-1-hexyn-3,6-diol [1] with alkali. Heating of glycol (I) with 40% potassium hydroxide solution led to evolution of acetylene which gave a characteristic precipitate of silver derivative; the residue was acetopropyl alcohol (2,4-dinitrophenylhydrazone with m. p. 143°).

Oxidation of glycol (I) with nitric acid. 8 grams of the glycol was dissolved in a mixture of 50 ml of conc. nitric acid and 10 ml of water, and the solution was heated on a water bath for 1/2 hour until commencement of a violent reaction accompanied by liberation of CO_2 and oxides of nitrogen. After an hour, the reaction mixture was neutralized with potassium carbonate solution and the neutral products were distilled into a solution of 2,4-dinitrophenylhydrazine. The melting point of the 2,4-dinitrophenylhydrazone was 124°; no depression in admixture with acetone 2,4-dinitrophenylhydrazone. The solution of the salts was evaporated to dryness and extracted with alcohol for elimination of resinous impurities. After the alcohol had been driven off, the residue was acidified with sulfuric acid and the volatile acids were distilled off with steam. Heating with silver carbonate gave the silver salt of a volatile acid (acetic).

Found %: Ag 64.70. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

A viscous, syrupy acid was isolated from the aqueous solution of the nonvolatile acids in the extractor and gave a 2,4-dinitrophenylhydrazone with m. p. 196-199°; a mixed test with the 2,4-dinitrophenylhydrazone of authentic levulinic acid did not give a depression. Consequently, the main product of oxidation was levulinic acid; acetic acid and acetone were formed as a result of its further oxidation. The residue of acetylene was oxidized to carbon dioxide.

Ozonization of 3-methyl-1-hexyn-3,6-diol (I). 3.1 g of the glycol was taken for ozonolysis. 1.44 g of ozone was used (124% reckoned on the triple bond). The ozonide was decomposed with water. Formic acid was determined in a part of the solution by Fincke's method [11] (40%). Steam distillation did not yield any neutral products. After acidification of the solution and distillation of the formic acid, the residue was extracted with ether in an extractor. The product gave a precipitate with a solution of 2,4-dinitrophenylhydrazine. Ozonization of 3-methyl-1-hexyn-3,6-diol could have been expected to lead to the lactone of α-methyl-α,δ-dihydroxyvaleric acid (X).



It is known that this type of lactone can react with phenylhydrazine to form a phenylhydrazide of the acid. Thus, valerolactone [12] reacts with phenylhydrazine to form the phenylhydrazide of hydroxyvaleric acid which, however, could not be isolated in a sufficiently pure form even after many recrystallizations.

The 2,4-dinitrophenylhydrazine derivative that we prepared was recrystallized with great difficulty, and its nitrogen content was rather lower than corresponded to the anticipated phenylhydrazide (15.51 instead of 17.83%). We therefore did not obtain adequate evidence of the identity of the compound.

The Raman spectrum of the glycol was prepared. It was necessary to work at 60° for this purpose because at the ordinary temperature in the light of the mercury lamp the viscous mass of glycol was observed to contain in suspension of small quantity of very fine crystals whose presence interfered with the plotting of the spectrum. The glycol did not crystallize, however, even after standing for 6 months, and the quantity of crystals had evidently not altered after this period of time. The 2108 cm^{-1} frequency, corresponding to the triple bond, was observed in the spectrogram.

Hydration of 3-methyl-1-hexyn-3,6-diol (I). 1 g of mercuric oxide was treated with a still hot mixture of 3.3 ml of conc. sulfuric acid and 100 ml of water; dropwise addition of 23 g of the glycol, dissolved in 25 ml of water, was made to the solution obtained; the mass was then heated for 1 hour at 80°, after which the volatile products were distilled off with steam. The distillate was salted out and extracted with ether to give about 1 g of substance with b. p. 127-133° and n_D^{20} 1.4380, which rapidly decolorized $KMnO_4$ solution and gave a 2,4-dinitrophenylhydrazine with m. p. 128-130°.

Found %: C 50.86; H 5.19; N 17.96. $C_{13}H_{16}O_5N_4$. Calculated %: C 50.65; H 5.19; N 18.18.

Results of analyses are in accord with data calculated for the 2,4-dinitrophenylhydrazone of the unsaturated compound that could be formed by dehydration of the ketoglycol by one of the schemes presented above.

The nonvolatile products were extracted with ether in an extractor for 7-8 days. Removal of the ether left 18 g (65%) of colorless crystals with m. p. 84-85°.

Found %: C 57.49; H 9.72; OH 22.90. M 165. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.59; OH 23.25. M 146.

The results obtained correspond to the formula of the ketoglycol. The ketoglycol gives a precipitate with m. p. 108-109° on treatment with 2,4-dinitrophenylhydrazine solution, not immediately but only after standing overnight.

Found %: C 50.82; H 5.16; N 18.09. $C_{13}H_{16}O_5N_4$. Calculated %: C 50.65; H 5.19; N 18.18. $C_{13}H_{18}O_6N_4$. Calculated %: C 44.44; H 8.66; N 17.17.

The composition of the hydrazone obtained thus corresponds not to a ketoglycol derivative but to a derivative of the unsaturated ketoalcohol. In the ketoglycol itself the carbonyl group was detected by plotting of the ultraviolet absorption spectrum in ethyl alcohol solution with the SF-4 spectrograph. Absorption maximum at 286 mμ, log ε 1.164 (x 1 cm, c 0.02).

Preparation of the ether of acetopropyl alcohol by reaction with dimethyl sulfate in alkali solution. Thirty-four g of acetopropyl alcohol was dissolved in 40 ml of 40% potassium hydroxide solution, and 46 g of freshly distilled dimethyl sulfate (b. p. 186-189°) was run in at such a rate that the temperature of the reaction mixture rose to 70-90°; thereupon it was heated on a water bath at 40-50° for 1-2 hours. The following day the precipitated salts were filtered off and the solution was extracted with ether; after drying followed by removal of the ether, the residue was distilled at 10 mm. The following fractions were obtained:

1st, b. p. 48-52°, 9 g, n_D^{20} 1.4134; 2nd, b. p. 52.5-53.5°, 6.5 g, n_D^{20} 1.4141.

The yield of crude product was approx. 40%. The compound was redistilled in a column at atmospheric pressure.

B. p. 152-155°, n_D^{20} 1.4147, d_4^{20} 0.9228; MR_D 31.46; calcd. 31.52.

Found %: C 61.72; H 10.34; OCH_3 27.10. M 104. $C_6H_{12}O_2$. Calculated %: C 62.07; H 10.34; OCH_3 26.72. M 116.

Acetopropyl alcohol methyl ether gave a 2,4-dinitrophenylhydrazone with m. p. 64° (from alcohol) and a semicarbazone with m. p. 124° (from alcohol).

Found (for the semicarbazone) %: C 48.58; H 8.61. $C_7H_{15}O_2N_3$. Calculated %: C 48.55; H 8.66.

The following other methods of synthesis of the methyl ether of acetopropyl alcohol were tried out.

1) Reaction of the bromide of acetopropyl alcohol with sodium ethoxide. This reaction gave about 70% of acetyltrimethylene.

2) Methylation of acetopropyl alcohol with methyl iodide in an alkaline medium. The original substances were recovered unchanged (part of the methyl iodide was hydrolyzed).

3) Methylation with methyl alcohol saturated with hydrogen chloride. A mixture of acetopropyl alcohol and its corresponding chloride were obtained.

The ultraviolet absorption spectrum of the methyl ether of acetopropyl alcohol in ethyl alcohol was plotted with the SF-4 spectrograph; thickness of absorbing layer x, 1 cm; c 0.02 m. Absorption maximum at 276 mμ and log ε 1.383.

Reaction of acetopropyl methyl ether with acetylene. The conditions of the A. E. Favorskii reaction were employed. Distillation of the product gave the following two fractions:

1st, b. p. 111-113° (38 mm), 17 g, n_D^{20} 1.4469; 2nd, b. p. 113.5° (37 mm), 35 g, n_D^{20} 1.4490.

Yield of crude product 85%. It was purified from traces of original methoxy derivative by treatment with saturated sodium bisulfite solution.

B. p. 102-102.5° (19 mm) 192-194° (760 mm), n_D^{20} 1.4494, d_4^{20} 0.9474, MR_D 40.29. $C_8H_{14}O_2\vDash$. Calculated 40.31.

Found %: C 66.93; H 9.84; OCH_3 21.88; OH 4.008. M 157. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86; OCH_3 21.83; OH 11.97. M 142.

The Raman spectrum of the prepared methoxy derivative of 3-methyl-1-hexyn-3,6-diol was plotted with Zeiss spectrograph at 25°. The frequency of 2107 cm^{-1} obtained is that of the characteristic vibration of the triple bond in monosubstituted acetylenes.

Analysis for hydroxyl by the Terent'ev method was carried out many times with various specimens, but the results were identical. 3-Methyl-6-methoxy-1-hexyn-3-ol therefore behaves anomalously not only towards ammoniacal silver oxide solution but also towards methyl magnesium iodide solution.

Hydrogenation of 3-methyl-6-methoxy-1-hexyn-3-ol. 1 g of the compound, 0.1 g of platinum black and 40 ml of anhydrous alcohol were taken. After 2 hours 336 ml of hydrogen had been taken up (101% of the theoretical calculated for the triple bond).

Ozonolysis of 3-methyl-6-methoxy-1-hexyn-3-ol. The quantity of ozone consumed was 104% of the theoretical, calculated for the triple bond. The ozonide was decomposed with water and the formic acid was determined by Fincke's method [11]; the amount found was 69.9%. No other acid products could be identified. Neutral products were not detected.

Hydration of 3-methyl-6-methoxy-1-hexyn-3-ol by the Kucherov method. 2.4 g of mercuric oxide was dissolved in a still mixture of 14 ml of sulfuric acid and 100 ml of water. 11 g of 3-methyl-6-methoxy-1-hexyn-3-ol was added dropwise to the cooled solution, and the temperature of the reaction mixture rose to 60-70°. When all had been added, the mass was heated to the boil for 2.5 hours. The reaction products were extracted with ether in an extractor; after drying and removal of solvent, the product was distilled in a vacuum of 18 mm. The following fractions were obtained:

1st, 92-97°, 0.8 g, n_D^{20} 1.4350; 2nd, 107-109°, 6.7 g, n_D^{20} 1.4360. The residue was a resin.

The yield of the 2nd fraction was 50% of the theoretical; it did not form derivatives with semicarbazide or 2,4-dinitrophenylhydrazone even on standing for many days; it slowly decolorized $KMnO_4$ solution; with ammoniacal silver solution it did not give a precipitate either in the cold or on boiling (indication of absence of starting product).

Constants of 3-methyl-6-methoxyhexan-2-one-3-ol: b. p. 107-109° (18 mm), n_D^{20} 1.4360, d_4^{20} 0.9913, MR_D 42.20; calcd. 42.32.

Found %: C 59.73; H 10.02; OCH_3 19.43; OH 10.92. M 159.8. $C_8H_{16}O_3$. Calculated %: C 60.00; H 10.00; OCH_3 19.04; OH 10.62. M 160.

The ultraviolet absorption spectrum of the methyl ether of the ketoglycol was plotted with the SF-4 spectrograph (x 1 cm; c 0.02 M); absorption maximum at 284 mμ and log ε 1.561.

The infrared spectrum of 3-methyl-6-methoxyhexan-2-one-3-ol was also plotted; the carbonyl group corresponded to the characteristic frequency of 1715 cm^{-1} (IKS-11 spectrometer).

SUMMARY

1. The acetylenic γ-glycol, 3-methyl-1-hexyn-3,6-diol, and its primary monomethyl ether, 3-methyl-6-methoxy-1-hexyn-3-ol, were synthesized.

2. Is was shown that both of these compounds do not react under ordinary conditions with ammoniacal silver oxide solution; only on boiling do they form light-yellow precipitates of the silver derivatives; the latter are soluble with difficulty in nitric acid; in the dry state they explode when being weighed out.

3. The presence of a triple bond in both of the compounds was demonstrated by hydrogenation, ozonization and oxidation, as well as by the Raman spectra.

4. The hydration of 3-methyl-1-hexyn-3,6-diol and its ether was studied. The resultant carbonyl compounds did not react with semicarbazide or 2,4-dinitrophenylhydrazine; the presence of a carbonyl group in both cases was established by the ultraviolet absorption spectra.

5. A 2,4-dinitrophenylhydrazone came down when the ketoglycol obtained by hydration of 3-methyl-1-hexyn-3,6-diol was stood with a sulfuric acid solution of 2,4-dinitrophenylhydrazine; it corresponded in composition to a derivative of the unsaturated ketoalcohol formed by dehydration of the ketoglycol.

6. It was shown that in the absence of 2,4-dinitrophenylhydrazine, the ketoglycol does not undergo dehydration under the influence of sulfuric acid of the same strength.

7. Methyl acetopropyl ether was prepared for the first time.

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Received December 30, 1956

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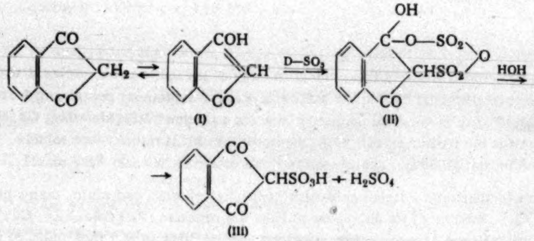
*Original Russian pagination. See C. B. Translation.

SULFONATION OF β-DIKETONES WITH DIOXANE SULFOTRIOXIDE

II. INDANDIONE-1,3-SULFONIC-2 ACID AND ITS SALTS

E. Iu. Gudrinietse, A. F. Ievin'sh and G. Ia. Vanag

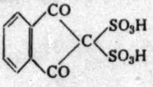
It was shown in a previous communication [1] that indandione-1,3 was easily sulfonated by dioxane sulfotrioxide (D-SO_3) giving indandione-1,3-sulfonic-2 acid. The sulfonation was carried out in a solution of 1,2-dichloroethane at room temperature. It has been suggested in the literature [2] that the sulfonation may proceed by way of the enol form (I) giving an addition product (II) whose hydrolysis yields the corresponding sulfonic acid, in our case



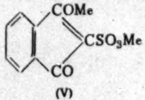
We did not, however, succeed in isolating the intermediate product (II). When indandione-1,3 is added to a solution of D-SO_3 in 1,2-dichloroethane, reaction takes place immediately, the solution becomes hot (water cooling!) and after 2-3 minutes indandione-1,3-sulfonic-2 acid (III) precipitates out. If the precipitate is dissolved in water, the solution does not give a reaction for the sulfate ion, which indicates that the intermediate product (II) was not formed.

It would appear that the reaction occurs directly with the hydrogen of the active methylene group in indandione-1,3; in other words indandione combines with the molecule of sulfuric anhydride to give indandione-1,3-sulfonic-2 acid (III).

If an excess of D-SO_3 is taken and the temperature is allowed to rise from 25 to 40° during the reaction, indandione-1,3-disulfonic-2,2 acid (IV) is formed; it is isolated as the sodium salt. It is interesting that the barium salt of this acid is very slightly soluble in water. Investigation of the disulfonic acid is proceeding and will form the subject of a separate report.



(IV)



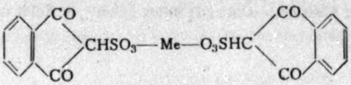
(V)

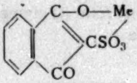
Indandione sulfonic acid (III) is a colorless crystalline substance which is hygroscopic in air. We did not succeed in recrystallizing the acid.

The sodium, potassium, lithium and ammonium salts were prepared by saturating the aqueous solution of indandione sulfonic acid with the appropriate chlorides. The indandione sulfonates obtained were yellowish or colorless crystalline substances, readily soluble in water, insoluble in alcohols and other organic solvents. The aqueous solutions of these salts are yellowish in color; when the solutions are acidified, the coloration disappears.

Treatment of the monosodium or monopotassium salt of indandione sulfonic acid gives the disodium (V, Me = Na) or dipotassium (V, Me = K) salts of this acid. They are precipitated by the addition of a small amount of ethanol. The dipotassium salt obtained corresponds in appearance and analytical findings to the same salt obtained by V. N. Ufimtsev [3]; however, no oxime could be obtained from it.

When an aqueous solution of indandione sulfonic acid is treated with strontium and barium ions, preferably at temperatures around zero, the corresponding salts (VI, Me = Sr, Ba) are obtained in crystalline form. The calcium salt could only be prepared in alcoholic solution; it is yellow and crystallizes with 2 molecules of water.


(VI)


(VII)

Salts obtained by neutralization of the aqueous solution of indandione sulfonic acid with carbonates of magnesium, calcium, strontium and barium are yellow crystalline substances containing 1 atom of metal per molecules of the acid. The salts obtained evidently have the structure (VII) (Me = Mg, Ca, Sr, Ba). The least water-soluble salt is the barium salt (0.10%), the strontium salt is rather more soluble (0.37%), and still more so the calcium salt (0.85%). The magnesium salt dissolves in water very readily.

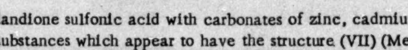
Neutralization of indandione sulfonic acid with carbonates of zinc, cadmium, manganese, nickel and cobalt gives salts of these substances which appear to have the structure (VII) (Me = Zn, Cd, Mn, Ni, Co). The zinc and cadmium salts are orange-yellow in color and crystallize with 2 molecules of water. The water of crystallization is removed at 150° and the salts become yellow.

The nickel, cobalt and manganese salts of type (VII) are of interest. They form complexes with pyridine. These may be promising with respect to preparation of complexes of a new type. Similar complexes of carboxylic acids are known in the literature [4]. How general this phenomenon might be will be revealed by further investigations.

The silver and lead salts (VII, Me = Ag, Pb) are also yellow and are formed in an acid medium. The silver salt is photosensitive and undergoes gradual decomposition with liberation of free silver.

Addition of organic bases to indandione sulfonic acid solution readily gives indandione sulfonates of these bases. The aniline, pyridine and quinoline salts thus obtained are colorless crystalline substances, very water-soluble; they are insoluble in alcohol and other organic solvents. They may be recrystallized from dilute ethanol.

Like other sulfonic acids [5], indandione sulfonic acid gives benzylthiouronium salt (VIII) with S-benzylthiourea; this salt crystallizes well and may be used for identification of indandione sulfonic acid.



$$\left[C_6H_5-CH_2-S-C\begin{matrix} NH_3 \\ NH \end{matrix} \right]^+ \left[C_6H_4\begin{matrix} CO \\ CO \end{matrix}CHSO_3 \right]^-$$

(VIII)

Indandione sulfonic acid, unlike nitroindandione [6], forms enolic salts easily. Some of these, for example the lead salt (VII, Me= Pb), are formed even in acid solution (pH 5). The enolic salts are less soluble than the sulfonic acid salts (V, VII), and are therefore more easily isolated. Despite this, no enolic salts have as yet been obtained with organic bases.

EXPERIMENTAL

Indandione-1,3-sulfonic-2 acid (III). 6 g (0.025 mole) dioxane sulfotrioxide (D-SO_3), was added to 7.3 g (0.05 mole) indandione-1,3 in 70 ml 1,2-dichloroethane, with stirring and water cooling so as to prevent the temperature from rising above 25°. A dark red solution was formed and after 2-3 minutes solid began to separate out. After 1.5 hours the precipitate was filtered off with suction, washed with anhydrous dichloroethane and placed in a vacuum desiccator. Yield of indandione-1,3-sulfonic-2 acid 7 g, m. p. 85-90°, very readily soluble in water, alcohol, dioxane and acetone, insoluble in ether, chloroform and carbon tetrachloride.

Found %: S 12.40. $C_9H_6O_5S$. Calculated %: S 14.18.

Salts of indandionesulfonic acid with 1 equivalent of metal. The sodium, potassium, lithium and ammonium salts were obtained by diluting the reaction mixture after sulfonation with water, separating the dichloroethane in a separating funnel and salting out the aqueous solution by appropriate chlorides. The salts were recrystallized from dilute ethanol.

Sodium salt. Yellowish prisms. Two molecules of water of crystallization which are removed at 100-105°. The salt begins to decompose and char at 115-120°.

Found %: Na 8.01; S 11.40; H_2O 13.15. $C_9H_5O_5SNa \cdot 2H_2O$. Calculated %: Na 8.09; S 11.28; H_2O 12.67.

Potassium salt. Colorless prisms.

Found %: K 14.70; S 12.35. $C_9H_5O_5SK$. Calculated %: K 14.79; S 12.12.

Lithium salt. Pale yellow fine hexagonal prisms.

Found %: Li 2.98. $C_9H_5O_5SLi$. Calculated %: Li 2.71.

Ammonium salt. Colorless prisms.

Found %: N 5.54. $C_9H_5O_5SNH_4$. Calculated %: N 5.74.

Calcium salt (VI, Me =Ca) was obtained by addition of an alcoholic solution of calcium chloride to an alcoholic solution of indandione sulfonic acid. Yellowish bipyramids; crystallized with 2 molecules of water, removed slowly on drying at 100° for 12 hours. Decomposed at 115-120°. Very easily soluble in water.

Found %: Ca 7.64; H_2O 6.77. $(C_9H_5O_5S)_2Ca \cdot 2H_2O$. Calculated %: Ca 7.60; H_2O 6.84.

Strontium salt (VI, Me = Sr). Obtained by addition of aqueous solution of strontium bromide and a small amount of alcohol to an alcoholic solution of indandione sulfonic acid. Crystals began to appear after 15 minutes at 0°. Colorless prisms. Decomposed at 120°. Easily distinguished from the corresponding calcium salt under the microscope.

Found %: Sr 15.85. $(C_9H_5O_5S)_2Sr$. Calculated %: Sr 16.28.

Barium salt (VI, Me = Ba). Obtained in the same way as the calcium salt, but precipitation with alcohol not necessary. Colorless prisms, easily dissolved in water. Decomposed at 120°.

Found %: Ba 23.49. $(C_9H_5O_5S)_2Ba$. Calculated %: Ba 23.38.

Salts of indandione sulfonic acid with 2 equivalents of metal (V, VII). These salts were obtained by neutralization of an aqueous solution of indandione sulfonic acid with carbonates until an alkaline reaction was reached.

Sodium salt (V). Obtained as mentioned above and also by addition of sodium carbonate solution to an aqueous solution of the monosodium salt and precipitation with a small amount of ethanol. Recrystallization from dilute ethanol gave bright yellow prisms, easily soluble in water (giving a yellow coloration, which disappears on acidifying the solution).

Found %: Na 14.10; H_2O 16.55; S 9.85. $C_9H_4O_5SNa_2 \cdot 3H_2O$. Calculated %: Na 14.19; H_2O 16.65; S 9.87.

Potassium salt (V). Yellow prisms. Crystallized with 2 molecules of water.

Found %: K 23.10; H_2O 10.67. $C_9H_4O_5SK_2 \cdot 2H_2O$. Calculated %: K 23.10; H_2O 10.64.

Silver salt (V) obtained on addition of silver nitrate to an aqueous solution of indandione sulfonic acid. Recrystallized from dilute ethanol. Yellow prisms. Gradual decomposition on exposure to light.

Found %: Ag 49.30. $C_9H_4O_5SAg_2$. Calculated %: Ag 49.03.

Calcium salt (VII, Me = Ca). Obtained by addition of calcium carbonate to an aqueous solution of indandione sulfonic acid until alkaline reaction and precipitated from solution by a small amount of ethanol, Recrystallized from 70-80% ethanol. Long, fine yellow needles. Solubility in water at 20° 8.55 g/liter, but recrystallization from water unsuccessful.

Found %: Ca 15.19. $C_9H_4O_5SCa$. Calculated %: Ca 15.16.

Strontium salt (VII, Me = Sr). Prepared similarly to the calcium salt. Recrystallized from water with addition of a little ethanol. Long, fine lemon-yellow prisms. Crystallized with 3 molecules of water. Solubility in water at 20° 3.74 g/liter.

Found %: Sr 24.02; H_2O 14.50. $C_9H_4O_5SSr \cdot 3H_2O$. Calculated %: Sr 23.90; H_2O 14.77.

Barium salt (VII, Me = Ba). Prepared as the preceding salts. Precipitated out without addition of alcohol. Solubility in water: 1.04 g/liter at 20°. Crystallized in yellow prisms on evaporating down the solution. Crystals contained 3 molecules of water.

Found %: Ba 33.17; H_2O 12.63. $C_9H_4O_5SBa \cdot 3H_2O$. Calculated %: Ba 33.00; H_2O 12.95.

Magnesium salt (VII, Me = Mg). Obtained as the preceding salts. Recrystallized from dilute ethanol. Canary-yellow prisms, containing 5 molecules of water of crystallization. On drying the latter gradually removed, the last molecule at 160°.

Found %: Mg 7.21; H_2O 24.90. $C_9H_4O_5SM$[illegible]$5H_2O$. Calculated %: Mg 7.18; H_2O 26.58.

Zinc salt (VII, Me = Zn). Recrystallized from dilute alcohol. Small tetrahedral orange-yellow prisms. Two molecules of water of crystallization, removed at 150°. Anhydrous salt lighter in color.

Found %: Zn 19.69; H_2O 11.18. $C_9H_4O_5SZn \cdot 2H_2O$. Calculated %: Zn 20.07; H_2O 11.06.

Cadmium salt (VII, Me = Cd). Recrystallized from water and a small amount of alcohol. Orange-yellow prisms. Crystallized with 2 molecules of water, removed at 150°. Anhydrous salt yellow.

Found %: Cd 29.85; H_2O 9.47. $C_9H_4O_5SCd \cdot 2H_2O$. Calculated %: Cd 30.17; H_2O 9.60.

Lead salt (VII, Me = Pb). Prepared from the monosodium salt and lead nitrate in aqueous solution. Precipitate dissolved in dilute nitric acid and the lead salt precipitated by neutralizing with ammonia to pH 5-6. Very slightly soluble in water. Yellow square plates.

Found %: Pb 48.40. $C_9H_4O_5SPb$. Calculated %: Pb 48.03.

Nickel salt (VII, Me = Ni). Prepared in the same way as the calcium salt. Recrystallized from dilute ethanol (1 : 1). Greenish-yellow very small prisms, 4 molecules of water of crystallization 2 of which (13.65%) were driven off at 105°, the remaining two at 150°.

Found %: Ni 15.87; S 8.76; H_2O 19.43. $C_9H_4O_5SNi \cdot 4H_2O$. Calculated %: Ni 16.53; S 9.02; H_2O 20.29.

Complex cobalt salt with pyridine. To an aqueous solution of indandione sulfonic acid was added cobalt carbonate until no more carbon dioxide was evolved. A brownish, water-insoluble precipitate was formed. Crystallization from very dilute pyridine gave long brownish-red crystals containing 2 molecules of pyridine and 1 molecule of water. A more convenient way of obtaining this complex consisted of addition to an aqueous solution of the monosodium salt of indandione sulfonic acid of cobalt nitrate and subsequent gradual addition of pyridine. Red crystals of the complex precipitated out immediately.

Found %: Co 12.12; N 6.14; S 6.97. $C_9H_4O_5SCo \cdot 2C_5H_5N \cdot H_2O$. Calculated %: Co 12.85; N 6.18; S 6.99.

Complex manganese salt with pyridine. Prepared similarly to the cobalt complex. Recrystallized from dilute pyridine (1 : 4). Red prisms. On exposure to air pyridine gradually left the molecule and the color of the crystals changed to yellow.

Found %: N 6.47; Mn 11.95; S 7.03. $C_9H_4O_5SMn \cdot 2C_5H_5N \cdot H_2O$. Calculated %: N 6.15; Mn 12.10; S 7.04.

Aniline salt. Prepared by addition of aniline to an alcoholic solution of indandione sulfonic acid. Recrystallized from dilute ethanol. Long colorless prisms. M. p. 145-148° (decomp.).

Found %: N4.39. $C_{15}H_{13}O_5NS$. Calculated %: N 4.44.

Pyridine salt. Similar to the aniline salt. Long colorless prisms (from dilute ethanol). M. p. 210-211° (decomp.).

Found %: N 4.89. $C_{14}H_{11}O_5NS$. Calculated %: N 4.59.

Quinoline salt. Similar to the aniline salt. Long colorless prisms (from dilute alcohol). M. p. 214° (decomp.).

Found %: N 4.14. $C_{18}H_{13}O_5NS$. Calculated %: N 3.95.

Benzylthiouronium salt (VIII). Prepared from the sodium salt of indandione sulfonic acid and benzylthiourea in alcoholic solution. Colorless prisms (from dilute ethanol). M. p. 192-194°.

Found %: N 6.82. $C_{17}H_{15}O_5S_2N_2$. Calculated %: N 7.17.

SUMMARY

1. Sulfonation of indandione with 1,3-dioxane sulfotrioxide under certain conditions gives both indandionemonosulfonic acid and the disulfonic acid. Reaction mechanism for sulfonation of indandione is given.

2. Unlike 2-nitroindandione, indandionesulfonic acid undergoes enolization easily.

3. It has been established that either the sulfo group alone or the sulfo group and the enol group may participate in the formation of salts of indandionesulfonic acid. A series of salts of both types has been prepared.

4. The cobalt, nickel and manganese salts of indandionesulfonic acid give complex compounds with pyridine.

5. Indandionesulfonic acid may be identified by its S-benzylthiouronic salt.

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Received December 24, 1956

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*Original Russian pagination. See C. B. Translation.

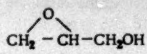
**In Russian.

REACTION OF HYDROGEN PEROXIDE WITH ALLYL ALCOHOL AND ACROLEIN IN THE PRESENCE OF TUNGSTIC ACID

P. G. Sergeev and L. M. Bukreeva

A number of investigations have recently been published in connection with the reaction of unsaturated compounds with hydrogen peroxide in the presence of catalysts. These have shown that hydrogen peroxide adds on across the double bonds [1-11].

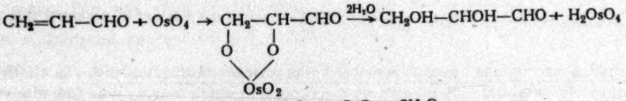
Milas [1] and Waters [12] consider that hydroxyl radicals are formed in this reaction and it is these radicals which add on across the double bonds. These authors' hypothesis has not, however, been confirmed experimentally. Nor has the view held by Mugdan [10] been proved; he considers that the reaction between hydrogen peroxide and allyl alcohol in aqueous solution and in the presence of tungstic acid is an ionic reaction. Crigee's work [13] merits attention; he showed that the interaction of unsaturated compounds with hydrogen peroxide in the presence of osmium tetroxide proceeds by way of osmic acid esters, which he succeeded in isolating from the reaction products. The hydroxyl derivatives are obtained by saponification of these esters.

The present work is concerned with studies of the reaction between allyl alcohol or acrolein and hydrogen peroxide in the presence of tungstic acid. The following sequence of reactions appears to take place in the case of allyl alcohol: hydrogen peroxide forms pertungstic acid with tungstic acid, pertungstic acid reacts with allyl alcohol at the double bond forming a glycidic alcohol ($H_2WO_5 + CH_2{=}CH-CH_2OH \rightarrow$  $CH_2-CH-CH_2OH$ $+H_2WO_4$) which is then hydrated to glycerol.

With acrolein, hydrogen peroxide reacts (in the presence of tungstic acid) almost exclusively at the carbonyl group, forming mainly acrylic acid.

According to the data of an American patent held by the Shell Company [11] the reaction between acrolein and hydrogen peroxide follows a different course in the presence of osmic anhydride. Hydrogen peroxide adds on across the double bond forming glyceraldehyde.

Such a direction of reaction is, evidently, a particular case of conversions studied by Crigee and apparently also proceeds by way of appropriate esters of osmic acid which are subsequently saponified. No peracids are formed and with respect to the interaction with acrolein the following course of the reaction must be suggested



$$CH_2{=}CH-CHO + OsO_4 \rightarrow \underset{O\diagdown\ \diagup O\ (OsO_2)}{CH_2-CH}-CHO \xrightarrow{2H_2O} CH_2OH-CHOH-CHO + H_2OsO_4$$

$$H_2OsO_4 + H_2O_2 \rightarrow OsO_4 + 2H_2O$$

In the presence of tungstic acid, however, pertungstic acid is evidently formed first and then oxidizes the acrolein carbonyl group

$$H_2O_2 + H_2WO_4 \longrightarrow H_2WO_5 + H_2O$$

$$CH_2{=}CH{-}CHO + H_2WO_5 \longrightarrow CH_2{=}CH{-}COOH + H_2WO_4$$

EXPERIMENTAL

Reaction of allyl alcohol with hydrogen peroxide in the presence of tungstic acid. To a 9% aqueous solution of allyl alcohol, warmed to 70°, was added with vigorous stirring perhydrol (10% excess over theoretical) in which tungstic acid (3% with respect to allyl alcohol) had been dissolved. The reaction products were analyzed for glycerol content by the Bertram method [14], for allyl alcohol by the bromide-bromate method, for hydrogen peroxide iodometrically and for oxides by the Deckert-Lubatti method [15].

During the first 10-15 minutes after mixing the reagents, the reaction mixture contained up to 2% (calculated for glycidic alcohol) of compounds containing the oxide group. Their amount gradually decreased and after 3 hours reached 0.05%. In order to isolate the glycidic alcohol the reaction mixture was cooled soon after mixing the reagents and treated repeatedly with ether. The solvent was distilled off and the residue vacuum-distilled.

B. p. 65-70° (2.5 mm), d_4^{20} 1.119, n_D^{20} 1.4350.

Literature data: d_4^{20} 1.115, n_D^{20} 1.4302 [16].

Found %: C 48.98; H 7.90. $C_3H_6O_2$. Calculated %: C 48.65; H 8.17.

The insufficient purity of the isolated glycidol is explained by certain difficulties in isolating it from the mixture in which it is present in small concentration and the ease with which it is hydrated at raised temperatures. Hydration takes place very slowly at room temperature, but becomes rapid at 70°. This evidently provides the rationale for hydroxylation of allyl alcohol with hydrogen peroxide in the presence of tungstic acid at a temperature of 70°.

Glycerol was isolated from the reaction mixture by distilling off water and fractionating the residue under vacuum. Tungstic acid was first removed from solution by passage through anion-exchange resins. Glycerol was obtained in concentration of 99.3%.

A small amount of carbonyl compounds is formed as a side product in this reaction; this is evidently racemic glyceraldehyde which can be formed by oxidation of glycerol with hydrogen peroxide (especially in the presence of traces of iron oxide).

Analysis of the precipitate of dinitrophenylhydrazone isolated on treating the reaction mixture with 2,4-dinitrophenylhydrazine solution gave the following results:

Found %: C 39.02; H 3.70; N 20.80. $C_9H_{10}O_6N_4$. Calculated %: C 40.00; H 3.70; N 20.74.

The possibility is not, however, excluded that a certain amount of isomeric dihydroxyacetone is formed.

The yield of glycerol reaches 95% (calculated on allyl alcohol), the amount of carbonyl side products from 3 to 5%.

Reaction between acrolein and hydrogen peroxide in the presence of tungstic acid. To a 10% aqueous solution of acrolein at 70° perhydrol (10% excess over theoretical) in which tungstic acid (3% with respect to acrolein) had been dissolved was added with vigorous stirring. The reaction mixture was maintained at this temperature for 2 hours; acrolein and water were then distilled off from the reaction products. Acrylic acid was determined in the residue with reference to two functional groups: double bond by the bromide-bromate method and carbonyl group by titration with 0.1 N solution of sodium hydroxide in the presence of phenolphthalein; the content of carbonyl compounds was determined by precipitation with dinitrophenylhydrazine (calculated for glyceraldehyde).

The main reaction product was acrylic acid whose yield exceeded 70% calculated on acrolein; only 1-2% carbonyl compounds was formed.

The results of one of the experiments are given below.

Acrolein taken (g)	Residue after distillation of most of the water (g)	Results of residue analysis (%)		Yield calculated on acrolein (%)	
		acrylic acid	carbonyl compounds	acrylic acid	carbonyl compounds
22.5	43.3	50.4* 49.8**	1.3	76.7	1.7

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*Bromide-bromate method

**Titration with 0.1 N NaOH

SUMMARY

1. A study was made of the interaction of hydrogen peroxide with allyl alcohol and acrolein in the presence of tungstic acid.

2. Precise data have been obtained on the sequence of events in these reactions.

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Scientific-Research Institute
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Products

Received December 26, 1956

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*In Russian.

**Russian translation.

SYNTHESIS OF QUINUCLIDINE-3-ACETIC ACID

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In recent years a large number of mono- and disubstituted derivatives of quinuclidine have been obtained. Some of these compounds have shown important biologic properties. The main starting materials for the preparation of substituted derivatives of quinuclidine have been various quinuclidine carboxylic acids. The presence of carboxylic groups in these compounds permitted preparation of compounds not previously known for the quinuclidine series: aldehydes [1], amino acids, urethanes [2], lactones [3], various substituted amines [4] etc.

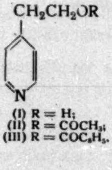
The compounds mentioned belong chiefly to 2-monosubstituted, 2,3- and 2,5 disubstituted derivatives of quinuclidine. Substituted quinuclidines with the substituents in position 3 have received less detailed study. In connection with this, the work of Lukes et al. [5] should be mentioned, since he studied preparation of 3-vinylquinuclidine, as well as work concerned with the synthesis of esters of quinuclidineol-3 [6] and quinuclidine-3-carboxylic acid [7].

The present work deals with the synthesis of quinuclidine-3-acetic acid which provides the opportunity for extending the investigation of 3-substituted derivatives of quinuclidine.

The starting material for the synthesis of quinuclidine-3-acetic acid was 4-(β-hydroxyethyl)-pyridine. This compound was obtained by condensation of a mixture of β- and γ-picolines with formaldehyde. 4-(β-hydroxyethyl)-pyridine was separated from the γ-di- and trimethylelpicolines formed at the same time by twice repeated vacuum distillation rather than by recrystallization of the picrate as proposed by Meisenheimer [8]. The yield of 4-(β-hydroxyethyl)-pyridine was 6-7% as against 1.2-1.5% shown by that author.

In order to carry out the proposed synthesis of quinuclidine-3-acetic acid it was necessary to effect the condensation of 4-(β-hydroxyethyl)-pyridine with chloral so as to obtain 1,1,1-trichloro-2-hydroxy-(pyridyl-4')-4-hydroxybutane. This condensation resulted in tarry products only, apparently as the result of formation not only of the addition product of chloral and 4-(β-hydroxyethyl)-pyridine but also of easily polymerized 4-vinylpyridine. It was proposed to replace the exceedingly reactive 4-(β-hydroxyethyl)-pyridine by acetoxy or benzoxy derivatives in which the ester group could be easily eliminated in the course of the synthesis.

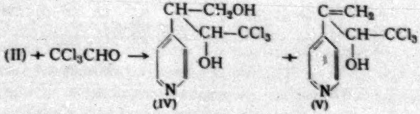
4-(β-acetoxyethyl)-pyridine (II) was obtained with an 83% yield on treating 4-(β-hydroxyethyl)-pyridine (I) with acetyl chloride in 10 times the volume of pyridine at a temperature not exceeding 10°.



(I) $R = H$;
(II) $R = COCH_3$;
(III) $R = COC_6H_5$.

Halving the amount of pyridine or its replacement by benzene lowered the yield of the acetoxy derivative by 50%. Acetylation of 4-(β-hydroxyethyl)-pyridine with acetyl chloride at a temperature above 10°, as well as by acetic anhydride, led to the formation of considerable amounts of 4-vinylpyridine. 4-(β-acetoxyethyl)-pyridine gradually turns viscous and brown when allowed to stand at room temperature. These phenomena are explained by conversion of the acetoxy derivative into 4-vinylpyridine which tends to polymerize and darken with time.

Condensation of 4-(β-acetoxyethyl)-pyridine (II) with chloral in benzene in the presence of piperidine acetate gave 1,1,1-trichloro-3-(pyridyl-4')-2,4-dihydroxybutane (IV) with a yield of about 10%. In addition to this substance an approximately equal amount of 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4 (V) was isolated.

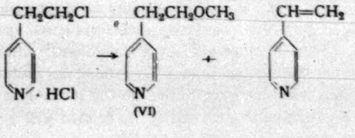


More prolonged heating of the reaction mixture (30 hours instead of 16 hours) leads to the exclusive formation of compound (V) with a yield of 30%. Condensation of (II) with chloral was also effected with pyridine and toluene as solvents, but only the unsaturated compound (V) was isolated in these cases.

4-(β-benzoxyethyl)-pyridine (III), obtained by interaction of 4-(β-hydroxyethyl)-pyridine with benzoyl chloride in aqueous alkali solution, decomposed on vacuum distillation with the formation of 4-vinylpyridine; consequently compound (III) was obtained in the pure state only in the form of the hydrochloride.

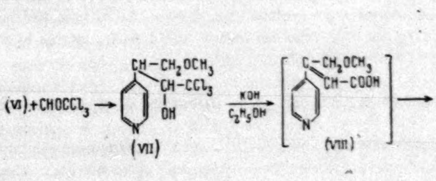
The data presented show that 4-(β-hydroxyethyl)-pyridine and its esters are easily converted into 4-vinylpyridine under the influence of such factors as time, temperature and chemical reagents.

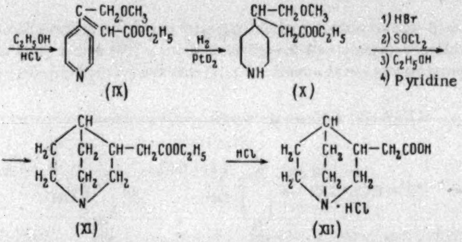
A more stable compound was found in 4-(β-methoxyethyl)-pyridine (VI). The latter was obtained by brief heating of 4-(β-chloroethyl)-pyridine hydrochloride with sodium methylate, the yield being 42%. In addition to compound (VI) a certain amount (11%) of 4-vinylpyridine was also formed.



Separation of these substances was easily achieved by fractional distillation under vacuum.

Conversion of 4-(β-methoxyethyl)-pyridine to quinuclidine-3-acetic acid was effected according to the following scheme.





4-(β-methoxyethyl)-pyridine was condensed with chloral in the presence of piperidine acetate; 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane (VII) was obtained. In this case, unlike the analogous reaction of 4-(β-acetoxyethyl)-pyridine with chloral, no formation of substituted 4-vinylpyridine was observed.

Compound (VII) was treated with an alcoholic solution of potassium hydroxide, the 4-methoxy-3-(pyridyl-4')-crotonic acid (VIII) formed was converted directly into the ethyl ester (IX). Reduction of pyridylcrotonic ester (IX) in the presence of platinum catalyst (according to Adams) at room temperature gave the ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid (X). In order to replace the methoxy group by halogen and to obtain the quinuclidine derivative, compound (X) was heated with 67% hydrobromic acid in a sealed tube at 110-120°. The 4-bromo-3-(piperidyl-4')-butyric acid thus formed was esterified and then subjected to cyclization in the presence of pyridine, giving the ethyl ester of quinuclidine-3-acetic acid (XI). Saponification of the latter gave quinuclidine-3-acetic acid (XII).

EXPERIMENTAL

4-(β-hydroxyethyl)-pyridine (I). 806 g of a mixture of β- and γ-picolines, 180 g formalin (approximately 40%) and 700 ml water were boiled for 16 hours. β-Picoline and unreacted γ-picoline and formaldehyde were removed by steam-distillation. The reaction liquid was evaporated down under vacuum to the remaining thick liquid consisting of 4-(β-hydroxyethyl)-pyridine and small amounts of γ-di- and trimethylolpicolines, was added a mixture of 200 ml ether and 200 ml chloroform. After 3-5 hours the ether-chloroform solution was poured off from the undissolved residue, containing tarry substances and γ-trimethylolpicoline, and dried over sodium sulfate. After distilling off the solvents the residue was vacuum distilled. Twice repeated distillation yielded 29.6 g (6.5% taking the mixture to contain 40% γ-picoline) 4-(β-hydroxyethyl)-pyridine. B. p. 140-141° (9 mm). Picrate m. p. 132.5-134° [8].

4-(β-acetoxyethyl)-pyridine (II). To a solution of 4 g 4-(β-hydroxyethyl)-pyridine in 40 ml anhydrous pyridine was added with stirring 2.82 g acetyl chloride. The temperature was maintained within the range 0-10°. After the addition of acetyl chloride the reaction mixture was stirred at this temperature for a further 1½ hours. 20 ml water and 40 ml 15% soda solution was then added and the mixture extracted with benzene. The benzene solution was dried over potassium carbonate, the solvent distilled off and the residue vacuum-distilled. Yield 4.5 g (83.8%). Colorless mobile liquid, easily soluble in organic solvents, with difficulty in water. B. p. 124° (8 mm), n_D^{18} 1.5022.

Found %: C 65.64; H 6.67; N 8.50. $C_9H_{11}O_2N$. Calculated %: C 65.50; H 6.67; N 8.49.

Hydrochloride – colorless crystals, m. p. 98-100°. At 117° the molten substance became cloudy, then solidified and melted at 238° (melting point of 4-vinylpyridine hydrochloride). Thus, on heating, hydrochloride (II) was converted into 4-vinylpyridine hydrochloride.

4-(β-benzoxyethyl)-pyridine (III). To a solution of 5 g 4-(β-hydroxyethyl)-pyridine in 12 ml of water was added 6.1 ml 40% aqueous solution of sodium hydroxide and then, with stirring, 6.9 g benzoyl chloride. After mixing the components, the reaction mixture was stirred for 1 hour and extracted with ether. The ethereal solution was dried over potassium carbonate, filtered and treated with 20% alcoholic solution of hydrogen chloride until an acid reaction to Congo. The crystals which separated out were filtered off, washed with ether and dried. Yield 6.4 g (60%) 4-(β-benzoxyethyl)-pyridine hydrochloride. Colorless crystals, easily soluble in water and alcohol, insoluble in ether, acetone. M. p. 121-123° (from a mixture of alcohol and ether).

Found %: N 5.76. $C_{14}H_{13}O_2N \cdot HCl$. Calculated %: N 5.32.

Condensation of 4-(β-acetoxyethyl)-pyridine with chloral. a) To a solution of 2.4 g 4-(β-acetoxyethyl)-pyridine and 2.1 g chloral in 15 ml anhydrous benzene was added 8 drops of piperidine and 6 drops of glacial acetic acid. The reaction mixture was heated at 80° for 16 hours; the mixture gradually turned a dark brownish color. On cessation of heating the benzene was distilled off under vacuum, the residue dissolved in 12 ml 7% hydrochloric acid and boiled for 10 minutes. The hydrochloric acid solution was cooled and treated with soda until an alkaline reaction to phenolphthalein; a large amount of tar separated out at this stage. The alkaline solution was extracted with benzene, the benzene solution dried over potassium carbonate, the solvent distilled off under vacuum and the remaining oily crystals triturated with ether. The crystals which separated out were filtered off, washed with ether and recrystallized from benzene. Yield 0.4 g (10%) 1,1,1-trichloro-3-(pyridyl-4')-2,4-dihydroxybutane (IV). Colorless crystals, easily soluble in chloroform, less so in ethyl acetate, benzene, acetone, alcohol, insoluble in water and in ether. M. p. 117-119°.

Found %: C 40.17; H 3.83; N 5.22; Cl 38.74. $C_9H_{10}O_2NCl_3$. Calculated %: C 39.93; H 3.70; N 5.17; Cl 39.20.

The ethereal mother liquor left after separation of crystals (IV) was treated with 20% alcoholic solution of hydrogen chloride until an acid reaction to Congo. The oil which separated out was washed by decantation with ether and triturated with a small amount of anhydrous alcohol. 0.4 g 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4-hydrochloride (V) separated out. Colorless crystals, easily soluble in water and alcohol, insoluble in ether, acetone, benzene. M. p. 153-154° (decomp.) from a mixture of alcohol and ether.

Found %: C 37.49; H 3.12; N 5.04; Cl' 12.14. $C_9H_8ONCl_3 \cdot HCl$. Calculated %: C 37.38; H 3.11; N 4.85; Cl' 12.27.

b) 8.35 g 4-(β-acetoxyethyl)-pyridine, 7.37 g chloral, 0.48 ml piperidine and 0.24 ml glacial acetic acid were heated at 80° for 30 hours. After treatment similar to that described in the preceding experiment, the benzene extract yielded 3.75 g (29.4%) 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-butene-4 (V). Colorless crystals, easily soluble in benzene, acetone, alcohol, insoluble in water and in ether. M. p. 128-129° (from benzene).

Found %: C 42.43; H 3.18; N 5.50; Cl 42.24. C_9H_8ONCl. Calculated %: C 42.77; H 3.17; N 5.54; Cl 42.24.

4-(β-methoxyethyl)-pyridine (VI). To an alcoholic solution of sodium methylate, obtained from 33 g sodium and 260 ml anhydrous methyl alcohol, was added with cooling a solution of 28 g 4-(β-chloroethyl)-pyridine hydrochloride in 200 ml anhydrous methyl alcohol. The reaction mixture was boiled for 1 hour; the solution, which was green when the components were mixed, turned a brownish color. After cooling, methyl alcohol saturated with hydrogen chloride was added to the reaction mixture until an acid reaction to Congo. The sodium chloride which precipitated out was filtered off and the alcoholic solution evaporated down under vacuum. The residue was dissolved in 30 ml water, 100 ml 15% soda solution added to it and the whole extracted with ether. The ethereal solution was dried over potassium carbonate, the ether distilled off and the residue distilled under vacuum at 8 mm. Two fractions were collected: 1st fraction, b. p. 65-80° (1.87 g) contained mainly 4-vinylpyridine; 2nd fraction, b. p. 80-92° (12.3 g) consisted of 4-(β-methoxyethyl)-pyridine and a small amount of 4-vinylpyridine. When the 2nd fraction was fractionated repeatedly 9.2 g (42.6%)

4-(β-methoxyethyl)-pyridine was obtained. B. p. 92-93° (10 mm). Colorless, mobile liquid, easily soluble in organic solvents, insoluble in water.

Found %: N 10.29. $C_8H_{11}ON$. Calculated %: N 10.22.

Picrate – yellow crystalline powder, easily soluble in acetone, alcohol, insoluble in water, ether. M. p. 93-95° (from alcohol).

Found %: C 46.27; H 4.21; N 15.28. $C_8H_{11}ON \cdot C_6H_3O_7N_3$. Calculated %: C 45.90; H 3.82; N 15.30.

1,1,1-Trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane (VII). 23.4 g 4-(β-methoxyethyl)-pyridine, 25.2 g chloral, 1.5 g piperidine and 0.8 ml glacial acetic acid were heated at 50-55° (in a water bath) for 29 hours. The reaction mixture was cooled, diluted with ethyl acetate, the crystals which separated out were filtered off and washed on the filter with anhydrous alcohol. Yield 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane 10.7 g [46.3% calculated on reacted 4-(β-methoxyethyl)-pyridine]. Colorless crystals, moderately soluble in alcohol, poorly soluble in ethyl acetate, insoluble in ether, water. M. p. 172° (from alcohol).

Found %: C 42.13; H 4.51; N 4.79; Cl 37.70. $C_{10}H_{12}O_2NCl_3$. Calculated %: C 42.18; H 4.22; N 4.92; Cl 37.43.

The ethyl acetate mother liquor was evaporated down under vacuum, the residue dissolved in ether, the ethereal solution filtered from tarry substances and dried with potassium carbonate. After the ether was distilled off, the substance was vacuum distilled. 12.3 g of original 4-(β-methoxyethyl)-pyridine was recovered.

Ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid (IX). To a solution of 10.7 g potassium hydroxide in 210 ml anhydrous alcohol was added 9 g 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane. The reaction mixture became homogeneous in the course of 1 hour; after an additional time, potassium chloride began to precipitate out from the solution. The reaction mixture was allowed to stand at room temperature for 15 hours; it was then heated for 2 hours at 40-50°, after which excess potassium hydroxide was precipitated by means of carbonic acid in the form of potassium bicarbonate. Inorganic salts were separated, alcohol distilled off under vacuum and 20 ml 7% alcoholic solution of hydrogen chloride was added to the residue and the whole boiled for 3 hours. Alcohol was then distilled off under vacuum, the residue treated with 20 ml 50% solution of potassium carbonate and extracted with ether. The ethereal solution was dried over potassium carbonate and after the ether was distilled off, the product was vacuum distilled. 4.4 g (63%) ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid was obtained. Colorless, mobile liquid, easily soluble in organic solvents, insoluble in water. B. p. 118-119° (0.1 mm).

Found %: C 65.43; H 6.94; N 6.35. $C_{12}H_{15}O_3N$. Calculated %: C 65.16; H 6.78; N 6.33.

Ethyl ester of 3-(piperidyl-4')-4-methoxybutyric acid (X). To a solution of 6.32 g ethyl ester of 3-(pyridyl-4')-4-methoxycrotonic acid in 60 ml anhydrous alcohol was added alcoholic solution of hydrogen chloride, containing 1.04 g hydrogen chloride, and 0.3 g platinum oxide. The reaction mixture was shaken with hydrogen at room temperature until the requisite amount of hydrogen (2870 ml) had been absorbed. The platinum black was then filtered off and the alcoholic solution evaporated down under vacuum. The hydrochloride of the ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid was obtained in the form of a noncrystallizing oil. Yield quantitative.

The hydrochloride of the ester was treated with an aqueous solution of potassium carbonate and converted to the base. B. p. 105-108° (0.1 mm). Colorless liquid, easily soluble in organic solvents, poorly in water.

Found %: C 62.23; H 10.10; N 6.00. $C_{12}H_{23}O_3N$. Calculated %: C 62.88; H 10.00; N 6.12.

Ethyl ester of quinuclidine-3-acetic acid (XI). 1.2 g hydrochloride of the ethyl ester of 3-(piperidyl-4')-4-methoxybutyric acid and 20 ml 67% hydrobromic acid were heated in a sealed tube at 110-120° for 12 hours.

evaporated down under vacuum. The residue was dried by thrice-repeated addition of benzene with subsequent vacuum distillation. The 3-(piperidyl-4')-4-bromobutyric acid hydrobromide was heated with 7 ml thionyl chloride for 6 hours at 60-65°. Excess thionyl chloride was then distilled off under reduced pressure; the chloroanhydride obtained was heated with 7 ml anhydrous alcohol for 3 hours. After the alcohol was distilled off, the ester hydrochloride was treated with 50% solution of potassium carbonate and the base extracted with ether. The ethereal solution was dried with potassium carbonate, the ether was removed and the residue treated by boiling with 5 ml pyridine for 2 hours. Pyridine was then distilled off under vacuum; the residue was treated with 4 ml 25% solution of potassium carbonate and extracted with ether. After the ether had been removed, the product was vacuum distilled twice. Yield 0.24 g (27%). Colorless, mobile liquid, readily soluble in water and organic solvents. B. p. 91-93° (0.15 mm).

Found %: N 7.29; 7.21. $C_{11}H_{19}O_2N$. Calculated %: N 7.11.

Quinuclidine-3-acetic acid. 0.12 g ethyl ester of quinuclidine-3-acetic acid and 2 ml 18% hydrochloric acid were boiled for 5 hours. The acid solution was decolorized with animal charcoal and evaporated down under vacuum. The oily crystals obtained were triturated with acetone, the precipitate filtered off, washed with anhydrous alcohol and recrystallized from a mixture of alcohol and ether. Colorless crystals, easily soluble in water, soluble in alcohol on heating, insoluble in ether, acetone. M. p. 238° (decomp.).

Found %: C 51.93; H 7.63. $C_9H_{15}O_2N \cdot HCl$. Calculated %: C 52.60; H 7.77.

SUMMARY

1. Quinuclidine-3-acetic acid was synthetized from 4-(β-hydroxyethyl)-pyridine by way of 4-(β-methoxyethyl)-pyridine, 1,1,1-trichloro-2-hydroxy-3-(pyridyl-4')-4-methoxybutane, ethyl ester of 4-methoxy-3-(pyridyl-4')-crotonic acid and ethyl ester of 4-methoxy-3-(piperidyl-4')-butyric acid.

2. Certain ethers and esters of 4-(β-hydroxyethyl)-pyridine were obtained. It was shown that 4-(β-hydroxyethyl)-pyridine and its esters were readily converted to 4-vinylpyridine under the influence of such factors as time, temperature, chemical reagents. 4-(β-methoxyethyl)-pyridine proved to be a much more stable compound.

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Received January 7, 1957

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* Original Russian pagination. See C. B. Translation.

HYDROGENATION IN THE PRESENCE OF COLLOIDAL PALLADIUM

IX. HYDROGENATION OF VINYLPROPYL- AND VINYLBUTYLACETYLENES

Kh. V. Bal'ian, Z. A. Lerman and L. A. Merkur'eva

In work carried out with the participation of one of us [1], a study was made of the hydrogenation of two homologs of vinylacetylene, viz. vinylmethyl- and vinylethylacetylene. It appeared interesting to investigate the hydrogenation of other substituted vinylacetylenes containing radicals with longer carbon chains.

With this aim in view, we investigated hydrogenation of two hydrocarbons – vinylpropyl- and vinylbutylacetylene – in the presence of colloidal palladium with and without addition of decelerator (p-thiocyanochlorobenzene).

The hydrogenation products were separated from the original hydrocarbon and the mixture of olefins and diolefins obtained was brominated. The bromides formed were separated by vacuum distillation into di- and tetrabromides. The ratio of olefins to diolefins formed during hydrogenation was judged by the amounts of di- and tetrabromides obtained.

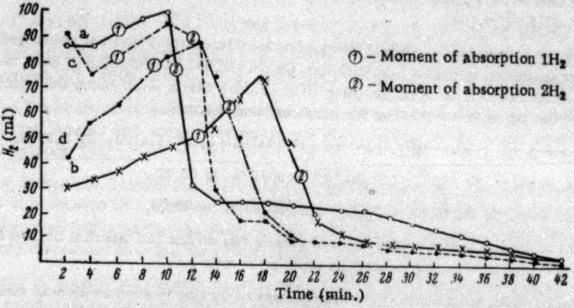
The olefins and diolefins were regenerated from the bromides by treatment with zinc in aqueous alcohol solution. Their structure was determined from physical constants, results of ozonolysis and condensation determined from physical constants, results of ozonolysis and condensation with maleic anhydride. It was found that the hydrocarbons under investigation differed little from their homologs – vinylmethyl and vinylethylacetylene [1] – studied earlier, with respect to the character of the curve for the rate of hydrogenation (see Fig.), site of initial addition of hydrogen, relative ease of addition of the first two molecules of hydrogen and the sharp drop in the rate of addition of the third molecule of hydrogen.

Formation of three hydrocarbons could be expected to result from the addition of one molecule of hydrogen to vinylalkylacetylene:

$$R{-}CH{=}CH{-}CH{=}CH_2 \quad \text{(I)}$$
$$R{-}C{\equiv}C{-}CH_2{-}CH_3 \quad \text{(II)}$$
$$R{-}CH{=}C{=}CH{-}CH_3 \quad \text{(III)} \quad R = n\text{-}C_3H_7 \text{ or } n\text{-}C_4H_9.$$

As in the previous cases, when $R = CH_3$ or C_2H_5, no hydrocarbons (II) and (III) were found. In addition to hydrocarbon (I) olefins were found which were formed during further hydrogenation of the alkadiene hydrocarbon. Hydrogenation of vinylpropylacetylene thus gave heptadiene-1,3 and a mixture of heptenes (chiefly heptene-1 and heptene-2) in the approximate ratio of 1:1.6. The same hydrocarbons were also obtained on hydrogenation of vinylpropylacetylene in the presence of p-thiocyanochlorobenzene (0.014% calculated on the weight of hydrocarbon), but, together with some slowing of the process (see Fig.) there was some change in the ratio between diene and olefin (1 : 0.94). This change indicated that the decelerator increased somewhat the selectivity of the hydrogenation process, by slowing the further conversion of diene into olefins.

When vinylbutylacetylene was hydrogenated with a ratio of 1 mole hydrocarbon : 1 mole hydrogen, octadiene-1,3 and a mixture of octenes were obtained in the ratio 1 : 1. The same hydrocarbons but in a ratio of



Catalytic hydrogenation of vinylbutylacetylene and vinylpropylacetylene.
a) Vinylbutylacetylene without decelerator; b) the same with decelerator;
c) vinylpropylacetylene without decelerator; d) the same with decelerator.

1.3 : 1 were obtained in the presence of p-thiocyanochlorobenzene amounting to 0.013% with respect to the weight of the hydrocarbon. It was noted that p-thiocyanochlorobenzene, amounting to 0.2% of the weight of the hydrocarbon, inhibited hydrogenation completely, acting as a catalyst poison; 0.1% of the decelerator caused very marked slowing of hydrogen addition, especially at the beginning of the process (Table 2). The positive effect of the decelerator on the selectivity of the hydrogenation process thus also manifested itself in the case of vinylbutylacetylene.

EXPERIMENTAL

Vinyl-n-propylacetylene (b. p. 108-109°, d_4^{20} 0.7654, n_D^{20} 1.4513) and vinyl-n-butylacetylene (b. p. 49-50° at 41-42 mm, 134-135° (760 mm) d_4^{20} 0.7749, n_D^{20} 1.4551) were synthetized from vinylacetylene and the appropriate alkyl halide in the presence of metallic sodium and liquid ammonia* [2].

Preparation of colloidal palladium and electrolytic hydrogen and description of the hydrogenation apparatus have been given earlier [3].

Hydrogenation of vinylpropylacetylene. a) In order to discover the character of complete hydrogenation and the effect of decelerator on the rate of hydrogenation of vinylpropylacetylene, parallel experiments were performed in which 1 g hydrocarbon, 2 ml (2 mg) Pd and 40 ml methanol were used without decelerator and with 0.4 mg (2 ml alcoholic solution) of p-thiocyanochlorobenzene at 17° and 765 mm. 753 ml was calculated for $3H_2$ Some slowing of the process caused by addition of p-thiocyanochlorobenzene** could be seen from comparison of curves (c and d in Fig.) plotted with time in minutes along the abscissa and amount of hydrogen absorbed in milliliters during equal periods of time along the ordinate. In the experiment without decelerator, 67% hydrogen ($2H_2$) added on during 12 minutes; with decelerator the same amount was taken up during 15 minutes. After this in both cases the rate of hydrogenation showed a marked fall. In the former case 96% hydrogen was absorbed in 72 minutes; in the latter only 93% hydrogen was absorbed in 108 minutes.

b) Vinylpropylacetylene was hydrogenated in the ratio 1 mole hydrocarbon : 1 mole hydrogen. 13.5 g hydrocarbon, 4 ml (4 mg) Pd, 175 ml methanol (18°, 787 mm) were taken. The calculated amount of 2H (3340 ml) added on during 51 minutes. 12 g hydrocarbon (88.8%) was isolated from the reaction mixture.

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* Synthesis of vinylpropylacetylene from propyl chloride gives a small yield (about 20%), whereas with propyl bromide the yield is 55-60%. Propyl bromide (b. p. 70-72°, d_4^{20} 1.3426, n_D^{20} 1.4330) was obtained from propyl acetate, H_2SO_4 (d 1.84) and potassium bromide with a yield of 60%.

** The corresponding tables with numerical data are omitted for purposes of space economy.

The following fractions were obtained on distillation with a fractionating column:

1st fraction 96-100°, 4.4 g, n_D^{20} 1.4174, d_4^{20} 0.7112; 2nd 100-104°, 3.2 g, n_D^{20} 1.4268, d_4^{20} 0.7279; residue 2.5 g, n_D^{20} 1.4516, d_4^{20} 0.7628.

The residue (25%) was seen to be the original hydrocarbon from its constants and was not subjected to further studies. For better separation of olefins from diolefins, the 1st and 2nd fractions (7.6 g) were brominated with 8 ml bromine in 40 ml chloroform. After distilling off chloroform with a water-pump the liquid bromides obtained were distilled twice at 4 mm. Two fractions were thus obtained:

1st 75-76°, 5.3 g, n_D^{20} 1.5030, d_4^{20} 1.5146; 2nd 133-134°, 5.4 g, n_D^{20} 1.5790, d_4^{20} 2.0958.

1st fraction. Found %: Br 62.60. $C_7H_{14}Br_2$. Calculated %: Br 62.02.

2nd fraction. Found %: Br 76.40. $C_7H_{12}Br_4$. Calculated %: Br 76.90.

The amounts of di- and tetrabromides obtained showed that olefins and diolefins obtained as the result of complete hydrogenation of vinylpropylacetylene were in the ratio 1.6 : 1.

From 5.0 g dibromide, 1.6 g olefin (83%) was regenerated by zinc in aqueous alcohol solution; the olefin had b. p. 95°, n_D^{20} 1.4050, d_4^{20} 0.7039.

0.33 g olefin was subjected to ozonolysis; the ozonides were decomposed and heated with a solution of β-naphthol. 0.2264 g dinaphtholmethane was obtained, corresponding to 22.3% heptene-1. Another sample of the olefin hydrocarbon was also subjected to ozonolysis; the ozonides formed were decomposed, the products of ozonolysis oxidized with $KMnO_4$ and the acids obtained subjected to prolonged extraction with ether and drying with anhydrous Na_2SO_4. After distilling off the ether the acid residues (2.5 g) were fractionally distilled from a small flask at ordinary pressure and two fractions were collected: 1st 115-116° (0.8 g) and 2nd 166-167° (0.6 g). The first fraction consisted of acetic acid, the second of valeric acid.

Taking into account the results of ozonolysis and the constants of the olefin [4] and the dibromide [5], it may be concluded that incomplete hydrogenation of vinylpropylacetylene resulted in a mixture of heptene-1 and heptene-2.

Of 5.1 g tetrabromide 1.1 g (91%) diolefin with b. p. 102-104°, n_D^{20} 1.4412, d_4^{20} 0.7387 was regenerated by zinc in aqueous alcohol solution.

Thera are no data in the literature concerning 1,2,3,4-tetrabromoheptane. References to heptadiene-1,3 are difficult to check in the original: n_D^{20} 1.4493 and d_4^{20} 0.7152 are given without citing the boiling point. Karasaev [6] gives the following values for an equal mixture of heptadiene-1,3 and heptadiene-1,4: b. p. 97-104°, n_D^{20} 1.4419 and d_4^{20} 0.7331, and for heptadiene-1,4: b.p. 100-101.5°, n_D^{20} 1.4370 and d_4^{20} 0.7270. The latter hydrocarbon is characterized in another source [7] by widely divergent data: b. p. 92°, n_D^{20} 1.420, d_4^{20} 0.7176.

In our case the tetrabromide could be formed either from heptadiene-1,3 or heptene-3, but the latter is excluded as it has b. p. 105-106°, 106-107°, n_D^{20} 1.415, d_4^{20} 0.7337 [8].

The diene obtained by us was condensed with maleic anhydride. Condensation took place to the extent of 41%, evidently at the expense of the trans-isomer only: 0.60 g heptadiene, 0.750 g maleic anhydride and 12 ml xylene were heated for 4 hours at 110-120° in a sealed ampoule. Maleic anhydride which did not enter the reaction was converted to maleic acid by boiling with water [6] and the acid was titrated with 22.6 ml NaOH (0.47 N), which corresponded to 0.50 g maleic anhydride which did not enter the condensation.

In order to elucidate the influence of the decelerator on the composition of the products of hydrogenation of vinylpropylacetylene with a ratio 1 mole hydrocarbon : 1 mole hydrogen, 29 g hydrocarbon was taken with 8 ml (8 mg) Pd, 240 ml methanol and 2 ml alcoholic solution p-thiocyanochlorobenzene (4 mg). Hydrogenation was carried out at 17° and 765 mm. The amount of hydrogen calculated for 2H was 7300 ml and was absorbed in 72 minutes. After isolation, purification, drying and repeated distillations at ordinary pressure the following fractions were collected:

1st 96-100°, 12.3 g, n_D^{20} 1.4220, d_4^{20} 0.7108; 2nd 100-104°, 6.2 g, n_D^{20} 1.4310, d_4^{20} 0.7260; residue 1.8 g, n_D^{20} 1.4510, d_4^{20} 0.7624.

The residue corresponded to the original hydrocarbon. The 1st and 2nd fractions together (18.5 g) were brominated with 20 ml bromine in 200 ml chloroform. After the chloroform was distilled off the liquid bromides were subjected to repeated vacuum distillation at 2mm, giving the following fractions:

1st 72-74°, 17.8 g, n_D^{20} 1.5006, d_4^{20} 1.5166; 2nd 130-131°, 30.1 g, n_D^{20} 1.5784, d_4^{20} 2.0952.

From 17.5 g dibromide 5.4 g (82%) olefin, b. p. 94-95°, n_D^{20} 1.4050 and d_4^{20} 0.7028 was regenerated. From 30 g tetrabromide 5.7 g (84%) diolefin, b. p. 102-104°, n_D^{20} 1.4404, d_4^{20} 0.7374, was regenerated.

The fact that the constants coincided for the dibromides, tetrabromides, regenerated olefins and diolefins obtained on hydrogenation with and without decelerator obviated the need for further investigation of these regenerated hydrocarbons.

The ratio of olefins and diolefins was calculated from the amounts of di- and tetrabromides obtained on hydrogenation with decelerator. The ratio was 0.94 : 1; the decrease in olefin and unreacted (unhydrogenated) original hydrocarbon indicated that the addition of p-thiocyanochlorobenzene favored the addition of hydrogen to the triple bond and hindered the addition to the double bond of the diolefins.

Hydrogenation of vinyl-n-butylacetylene. a) In order to elucidate the nature of complete hydrogenation and the effect of substituent on the rate of hydrogenation of vinylbutylacetylene, parallel experiments were set up: 1.0619 g hydrocarbon, 2 ml (2 mg) Pd, 40 ml methanol and 1.0930 g hydrocarbon; 2 ml (2 mg) Pd, 40 ml methanol and 0.2 ml alcoholic solution of p-thiocyanochlorobenzene (0.4 mg),[*] in both cases at 22° and 750 mm. The amount of hydrogen calculated for the first experiment ($3H_2$ – 726 ml) was absorbed in 36 minutes, while in the second experiment only 85% hydrogen calculated for $3H_2$ (753 ml) was taken up in 90 minutes.

The effect of the decelerator can be seen by comparing curves a and b in the Figure.

b) Vinylbutylacetylene was hydrogenated in the ratio 1 mole hydrocarbon : 1 mole hydrogen at 18° and 787 mm. The results are given in Table 1.

TABLE 1

Expt.	Amount hydrocarbon (g)	Amount methanol (ml)	Amount colloidal Pd (ml)	Calculated 2H (ml)	Time (min.)
I	20.384	225	15 (15 mg)	4390	24
II	19.060	200	10 (10 mg)	4100	27

The reaction masses of the two experiments were combined and from this mixture was isolated 33.7 g (85.5%) crude product. After drying over fused $CaCl_2$ 31.6 g hydrocarbon was fractionally distilled at normal pressure and a fraction with b. p. 126-131°, n_D^{20} 1.4317, d_4^{20} 0.7428 was collected, amounting to 25.7 g. The residue in the distilling flask (3.8 g, 13%) had n_D^{20} 1.4596, d_4^{20} 0.7931, i.e., was apparently somewhat contaminated original hydrocarbon. It was not investigated further.

In order to separate the olefins from diolefins, 25.7 g of the product was brominated with 25 ml bromine in 125 ml chloroform. After distilling off the chloroform and repeated fractional distillations under vacuum (3-4 mm) two fractions were collected:

1st 83-84°, 21.8 g, n_D^{20} 1.4985, d_4^{20} 1.4586; 2nd 145-147°, 35.9 g, n_D^{20} 1.5722, d_4^{20} 1.9768.

1st fraction. Found %: Br 58.36. $C_8H_{16}Br_2$. Calculated %: Br 58.82.

2nd fraction. Found %: Br 74.43. $C_8H_{14}Br_4$. Calculated %: Br 74.41.

According to the di- and tetrabromides obtained, the calculated ratio between olefins and diolefins was approximately 1 : 1.

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[*] Experiment with 1 ml solution of p-thiocyanochlorobenzene (2 mg) failed; no hydrogen was absorbed over a period of 40 minutes. With 0.5 ml p-thiocyanochlorobenzene (1 mg) hydrogen began to be absorbed only 20 minutes after the start of the experiment and only 75% of hydrogen calculated for $3H_2$ was taken up in the course of 153 minutes.

The tetrabromides yielded on freezing 5 g solid product with m. p. 66° (from methanol).

21 g dibromide, treated with zinc in aqueous alcohol solution, yielded 8.1 g (94%) hydrocarbon which gave on distillation at normal pressure 6 g hydrocarbon with b. p. 122-123°, n_D^{20} 1.4139, d_4^{20} 0.7244. Residue 1.4 g.

0.28 g olefin, after decomposition of its ozonides, gave with β-naphthol 0.2012 g dinaphtholmethane, which indicated the presence of about 26% octene-1 in the olefins. 3.8 g olefin was ozonized, the ozonides decomposed and the decomposition products converted to acids by oxidation with $KMnO_4$. The acids were extracted with ether by continuous extraction. Ether was distilled off (fractionating column), the residue (8 g) distilled under vacuum (water-pump). Four fractions were obtained: 1st 33-45° (68 mm), 2nd 45-80° (68-52 mm), 3rd 80-115° (52-30 mm), 4th 115-132° (30-29 mm).

In the 1st and 2nd fractions acetic acid was found after second fractional distillation, in the 3rd propionic acid and valeric acid, and in the 4th caproic acid (unlike valeric acid, caproic acid gave a white crystalline precipitate with zinc acetate). Ozonolysis results indicate that the olefins obtained on hydrogenation of vinylbutylacetylene are a mixture of octene-1, octene-2 and octene-3.

There are data in the literature concerning various octenes [4] and 1,2-dibromooctane [9]; there is no information about 2,3- and 3,4-dibromooctanes.

Comparison of our data and literature data confirms the conclusions made by us on the basis of ozonolysis results.

25.3 g tetrabromide treated with zinc in aqueous alcohol solution yielded 3.2 g hydrocarbon. Distillation of the latter at normal pressure at 130-131° gave 2.1 g of a product with n_D^{20} 1.4499, d_4^{20} 0.7578; residue 1 g.

There are no data in the literature with respect to octadiene-1,3 and 1,2,3,4-tetrabromooctane. On the basis of considerations mentioned above in connection with heptadiene and tetrabromoheptane it may be concluded that the diolefin obtained by us on hydrogenation of vinylbutylacetylene was octadiene-1,3 and the bromide correspondingly 1,2,3,4-tetrabromooctane.

The effect of the decelerator on the composition of hydrogenation products of vinylbutylacetylene with a molar ratio of hydrocarbon and hydrogen can be seen from the following experiments: 30.6 g vinylbutylacetylene was hydrogenated in the presence of 10 ml colloidal Pd (10 mg Pd), 250 ml methanol, 2 ml alcoholic solution p-thiocyanochlorobenzene (4 mg) at 21° and 755 mm. The calculated amount of hydrogen (2H) — 6880 ml — was taken up in 234 minutes (Table 2).

TABLE 2

Time (min.)	25	50	75	100	125	150	175	200	210	220	224	228	232	234
Vol. H (ml)	260	423	544	649	762	892	1061	1364	1825	3170	3850	5565	6280	6880
% H_2	3.8	6.1	7.9	9.5	11.0	12.9	15.4	19.8	26.6	46.0	56	80.7	91	100

The reaction mixture yielded 23.5 g hydrocarbon, fractional distillation of which gave 17.4 g product with b. p. 126-129°, n_D^{20} 1.4348, d_4^{20} 0.7431. Residue consisted of 4 g substance with n_D^{20} 1.4578, d_4^{20} 0.7829 (somewhat impure original hydrocarbon).

In another experiment, 17.92 g vinylbutylacetylene, in the presence of 5 mg Pd and 3 mg p-thiocyanochlorobenzene, gave after hydrogenation 9.55 g hydrocarbon with b. p. 126-129°, n_D^{20} 1.4347, d_4^{20} 0.7433 and a residue (3.4 g) with n_D^{20} 1.4548, d_4^{20} 0.7776 (original hydrocarbon).

Both samples of hydrocarbons combined (26 g) were treated with 24 ml bromine in 240 ml chloroform. After distilling off the solvent and repeated fractional vacuum distillations the following were obtained: 20.0 g dibromide with b. p. 92° (6 mm), n_D^{20} 1.4989, d_4^{20} 1.4585 and 41.2 g tetrabromide with b. p. 157-161° (6 mm), n_D^{20} 1,5722, d_4^{20} 1.9766.

The amount of bromides shows that the ratio of olefins to diolefins is 1 : 1.3.

Twenty g dibromide, treated with zinc in aqueous alcohol solution, yielded 6 g crude olefin which, on distillation gave 4 g of product with b. p. 122-123°, n_D^{20} 1.4139, d_4^{20} 0.7249; residue 1.5 g.

41.0 g tetrabromide, similarly treated, gave 7.7 g hydrocarbon which on distillation gave 4.1 g hydrocarbon with b. p. 130-131°, n_D^{20} 1.4500, d_4^{20} 0.7566, residue 2 g.

Addition of p-thiocyanochlorobenzene thus did not alter the composition of the reaction products obtained on hydrogenation of vinylbutylacetylene but retarded markedly (Table 2) the process of hydrogenation itself and changed the ratio of olefins to diolefins, increasing the yield of the latter.

SUMMARY

1. It was shown that in hydrogenation of vinylpropyl- and vinylbutylacetylene in the presence of colloidal palladium, the addition of hydrogen occurs at the triple bond as in the case of vinylmethyl- and vinylethylacetylene, with simultaneous further hydrogenation of the 1,3-dienes formed to the corresponding ethylene hydrocarbons.

2. It was established that the addition of a small amount of p-thiocyanochlorobenzene enhanced the selectivity of hydrogenation.

3. Octadiene-1,3, 1,2,3,4-tetrabromoheptane and tetrabromooctane were characterized for the first time; more precise constants are given for heptadiene-1,3.

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The Lensovet Leningrad Technological Institute Received January 4, 1957

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*Original Russian pagination. See C. B. Translation.

**Russian translation.

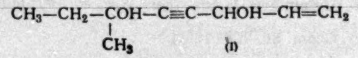
SYNTHESIS OF 6-METHYLOCTENE-1-YNE-4-DIOL-3,6 AND 7-METHYLOCTENE-2-YNE-5-DIOL-4,7 AND THEIR CATALYTIC HYDROGENATION

A. I. Nogaideli, K. Ia. Dzagnidze and R. Papava

We established in a previous communication [1] that the magnesium bromo derivative of dimethylacetylenylcarbinol reacted normally with acrolein at -7° to form ene-yne glycol— 6-methylheptene-1-in-4-diol-3,6. This ene-yne glycol, in the presence of colloidal palladium, adds on energetically 4 atoms of hydrogen, the last 2 atoms of hydrogen being added on more slowly [1].

It seemed interesting to synthetize other homologs of this class and to study the character of hydrogenation in the presence of catalysts.

6-Methyloctene-1-yne-4-diol-3,6 (I) was synthetized by the Zh. I. Iotsich method from methylethylacetylenylcarbinol and acrolein.



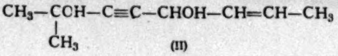
$$CH_3-CH_2-\underset{\underset{CH_3}{|}}{C}OH-C\equiv C-CHOH-CH=CH_2$$

(I)

Study of the hydrogenation reaction showed that in the presence of platinum black the rate of reaction of hydrogenation gradually decreased and there was no discontinuity after the addition of two or four atoms of hydrogen, although the first 2 atoms of hydrogen added on more slowly. In the presence of colloidal palladium, however, the eninglycol behaved like the first homolog [1], i.e., it added on the first 4 atoms of hydrogen more energetically with a sharp break and much slower addition of the last 2 atoms of hydrogen.

The product of exhaustive hydrogenation (over Pt and Pd) is a mobile oil. Analysis confirms that this substance is a saturated glycol 3-methyloctandiol-3,6.

Crotonaldehyde and dimethylacethylenylcarbinol gave a second eninglycol 7-methyloctene-2-yne-5-diol-4,7 (II).



$$CH_3-\underset{\underset{CH_3}{|}}{C}OH-C\equiv C-CHOH-CH=CH-CH_3$$

(II)

Hydrogenation of this substance in the in the presence of colloidal palladium showed a sharp change in the rate of reaction soon after the addition of two atoms of hydrogen. Hydrogenation proceeds even more slowly when platinum black is used.

Treatment of the hydrogenation product yields a colorless fairly thick oil, analysis of which confirms that it is the saturated glycol 2-methyloctandiol-2,5.

EXPERIMENTAL

Synthesis of 6-methylocten-1-yne-4-diol-3,6. The glycol was prepared in the usual way from 12 g magnesium, 56 g ethyl bromide, 21 g methylethylacetylenylcarbinol and 25 g acrolein. Yield 60.67%.

b. p. 144-145° (20 mm), d_{17}^{17} 0.9947, n_D^{17} 1.4850, MR_D 44.37; calc. 44.34.

Found %: C 70.04; H 8.92; OH 21.10. $C_9H_{12}(OH)_2$. Calculated %: C 70.10; H 9.00; OH 22.07.

Synthesis of 7-methylocten-2-yne-5-diol-4,7. The glycol was obtained from 12 g magnesium, 56 g ethyl bromide, 21 g dimethylacetylenylcarbinol and 35 g freshly distilled crotonaldehyde. The main reaction product distilled over at 100-108° (4 mm). Yield 18.5 g (26%).

d_{20}^{20} 1.0280, n_D^{20} 1.5210, MR_D 45.90; calc. 44.29.

Found %: C 69.48; H 10.9; OH 22.07. M 153.1 (cryoscopy) $C_9H_{12}(OH)_2$. Calculated %: C 70.12; H 9.9; OH 23.99. M 154.

Hydrogenation of 6-methylocten-1-yne-4-diol-3,6. Catalytic hydrogenation of the glycol was carried out in 50 ml ethyl alcohol. Results of hydrogenation are given in Table 1.

Saturated glycol 3-methyloctandiol-3,6 distilled over at 119-122° (4 mm).

d_{20}^{20} 0.9742, n_D^{20} 1.4643, MR_D 46.53; calc. 46.81.

Found %: C 67.80; H 12.50; OH 21.00. M 165 (cryoscopy) $C_9H_{18}(OH)_2$. Calculated %: C 67.50; H 12.59; OH 21.25. M 160.

TABLE 1

Expt. No.	Name of glycol•	Catalyst	Catalyst sample (mg)	Amount hydrogen (ml)		
				calc.	found	Uptake every 6 min.
1	6-Methylocten-1-yne-4-diol-3,6	Pt black	750	760	763	290. 190. 154. 105. 70. 15. 5. 2. 2. 1.
2	The same	Colloidal Pd	3	760	762	385. 209. 76. 42. 19 etc.; a total of 762 ml added on in 48 min.

• Sample of glycol in both experiments was 1.54 g.

TABLE 2

Expt. No.	Name of glycol	Sample of glycol (g)	Catalyst	Amount catalyst (mg)	Amount of hydrogen (ml)		
					calc.	found	Uptake every 6 min.
1	Methylocten-2-yne-diol-4,7	1.547	Colloidal Pd	50	761	765.	178, 118, 56, 40 etc.; a total of 765 ml added on in 240 min.
2	The same	1.516	Pt black	750	754	755	Hydrogenation proceeded very slowly and 20 hrs. were required for the absorption of 755 ml hydrogen.

Hydrogenation of 7-methylocten-2-yne-3-diol-4,7. Catalytic hydrogenation of the glycol was carried out in 50 ml ethyl alcohol. Results of hydrogenation are given in Table 2.

After treatment of the hydrogenation product the main fraction – 2-methyloctandiol-2,5 distilled over at 116-120° (4 mm).

d_{20}^{20} 0.9645, n_D^{20} 1.4668, MR_D 46.04; calc. 46.81.

Found %: C 67.25; H 12.10; OH 19.50. M 158.2 (cryoscopy). $C_9H_{18}(OH)_2$. Calculated %: C 67.50; H 12.50; OH 21.25. M 160.

SUMMARY

1. Two enin glycols were obtained: 6-methylocten-1-yne-4-diol-3,6 (I) and 7-methylocten-2-yne-5-diol-4,7 (II), which have not been described in the literature.

2. It was shown that the first glycol, in the presence of colloidal palladium, added on energetically 4 atoms of hydrogen with a subsequent change in the rate of reaction of hydrogenation.

3. In the presence of platinum black the rate of hydrogenation of both glycols gradually slowed down with no abrupt change in the rate of reaction after addition of 2 and 4 atoms of hydrogen.

4. The second glycol underwent hydrogenation much more slowly than the homologs described by us previously, and unlike the latter added on fairly energetically only 2 atoms of hydrogen.

In the course of this work, saturated glycols 2-methyloctandiol-2,5 and 3-methyloctandiol-3,6 were isolated and characterized.

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Received February 18, 1956

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*Original Russian pagination. See C. B. Translation.

INVESTIGATION OF LIGNIN IN HUSKS OF COTTON SEEDS

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The composition of the cotton seed husks has been studied by a number of workers [1-7]. These works show that the composition of the husk depends on the sort of cotton, degree of its ripeness, amount of lint on the seeds etc. The amount of separate components in the husk fluctuates considerably [6]: ash 2-2.85, pentosans 21.6-27.6, cellulose 36-48.5, lignin 19.6-32, oils and resins 2.1-3.8, uronic acids 4.4-5.5, proteins 3-9%. The methoxyl group content of the husks is 0.98-1.87%.

The data cited show that despite the considerable lignin content of the husks, the amount of methoxyl groups is one-third to one-quarter of that found in the wood of conifers, and in deciduous wood it is 3.5-4.5 times higher than in the husks. This indicates either that the lignin in cotton seed husks is very different in its composition from wood lignins or that its content in the husks is much lower than in wood. In the latter case the isolated lignin is contaminated by products of carbohydrate humification.

In order to elucidate these questions an investigation of the cotton seed husk lignin was undertaken. Lignin was isolated from the husks by various means. Comparison was made of the yields and analyses of the lignins obtained. In addition, oxidation of husks with nitrobenzene and alkali was carried out.

Husks from ripe cotton seeds from the Ferganskii Hydrolysis Plant were used for obtaining lignin.

The husks were covered with lint and had the following composition: ash 2.31%, resinous substances 1.42%, lignin according to Koenig 33.35%, OCH_3 1.50%, pentosans 25.29%, lint ~20%.

Lignin from husks twice extracted with dichloroethane was isolated: 1) according to the copper-ammonia method of Freudenberg [8] modified to the extent that, owing to the marked viscosity of the cellulose solution on initial treatment, the amount of copper-ammonia solution was increased to 4 liters per 100 g husks; 2) by the hydrochloric acid method lignin was isolated from the husks both after treatment with 5% NaOH and without alkaline treatment; 3) by precipitation of lignin with acid from alkaline solution obtained by treating dichloroethane-extracted husks with 5% solution of NaOH and separation of lignin from hemicelluloses by treatment of the precipitate (obtained by acidifying the solution) with alcohol.

The yields and composition of the lignins are presented in the table which shows that lignins isolated by the classic methods from cotton husks are markedly different from wood lignins obtained by the same methods. The methoxyl group content of these lignins is considerably lower than of wood lignins.

In order	Method of isolation	Yield, dry husks (%)	OCH_3 in lignin (%)	Content in lignin (%)	
				C	H
1	Copper-ammonia method	8	3.99	57.14	5.07
2	Hydrochloric acid method	17	4.28	59.04	4.62
3	Lignin isolated by the Koenig method	33.35	3.66		
4	Alkaline lignin	1	9.64	56.13	5.65

By oxidizing cotton husks with nitrobenzene and alkali a mixture of aldehydes was obtained. Their yield from dichloroethane-extracted husks was 1.58% (1.98% with reference to husks without lint and 4.73% with reference to Koenig lignin). The methoxyl group content of the aldehydes was 26.4% and crystals of vanillin were deposited after a period of standing.

Paper chromatography revealed the presence of vanillin and syringic aldehyde. The methoxyl group content of the aldehydes indicates that syringic aldehyde and vanillin are present in the mixture in the ratio 1.1 : 1.4. No n-hydroxybenzaldehyde was found in the aldehyde mixture.

The aldehyde composition shows that the "natural lignin of cotton seed husks is close to lignin of deciduous wood. However, husks yield much less lignin than the wood of deciduous plants. Investigation of cotton seed husk lignin is continuing.

EXPERIMENTAL

Isolation of lignin by the copper-ammoniacal method. Cotton seed husks were extracted twice with dichloroethane. The extracted husks were treated twice with a 5% aqueous solution of sodium hydroxide over a period of 24 hours at room temperature, with shaking; they were then washed with water, dilute acetic acid and again with water. Air-dried husks (without preliminary boiling with 1% H_2SO_4) were shaken for 12 hours with copper-ammoniacal solution in a flask filled to the top with the solution.

4000 ml solution (containing 1.3 g copper per 100 ml) was used for 100 g husks. The undissolved part of the husks was filtered off, washed with ammonia, water, dilute hydrochloric acid and again with water. The residue was boiled with 1% sulfuric acid and after drying again shaken with copper-ammoniacal solution (750 ml per 100 g). Boiling with 1% solution of sulfuric acid and treatment with copper-ammoniacal solution were repeated once again. The lignin obtained was in the form of a dark powder: yield 8%.

Alkaline lignin. The dark reddish-brown solution obtained by treating the husks with 5% solution of sodium hydroxide (after extraction with dichloroethane) was acidified to Congo, when a gelatinous precipitate came down. The precipitate was filtered off, washed with water and then treated with ethyl alcohol at room temperature. The alcohol was removed from the extract and a fine pale-brown powder was obtained in the residue. Its yield was 1% of the husk weight.

Oxidation of the husks with nitrobenzene and alkali. The extracted husks (100g) were mixed with 2 N solution of sodium hydroxide (1200 g) and nitrobenzene (100 g). The mixture was heated at 160° for 3 hours in an autoclave, with stirring. The contents of the autoclave were then transferred to a flask from which the nitrogen-containing substances were removed by steam-distillation. After cooling, the contents of the flask were filtered and the clear filtrate neutralized with sulfuric acid. 20 ml concentrated sulfuric acid was then added and the pH of the solution brought to 7.3 by the addition of Na_3PO_4. The mixture was extracted with trichloroethylene. The extract was shaken with 5% solution of sodium bisulfite. The bisulfite solution was acidified with sulfuric acid and the SO_2 driven off by gentle heating of the mixture on a water bath and passing CO_2 through it. After this the solution was extracted with ether. The ethereal extract was dried and the ether distilled off. In the residue was a product which was in the form of pale-yellow oil which tended to thicken and had a strong odor of vanillin. Fine needles of crystalline vanillin appeared on the surface, after a period of standing. Yield of aldehydes 1.58 g.

Paper chromatographic investigation of the aldehyde mixture. "Crab paper" (parchment-like base) prepared at the Leningrad Volodarskii Paper Mill No. 2 was used for this investigation. The developing solvent for the aldehydes was the mixture: ligroin + n-butyl alcohol + water in the ratio 6 : 1 : 1. The position of the aldehydes on the paper was found with the help of 0.2% solution of 2,4-dinitrophenylhydrazine in 2 N HCl.

SUMMARY

1. The husks of cotton seeds contain considerably less methoxyl groups than wood; this also applies to lignin isolated from cotton husks as compared with isolated wood lignins.

This means that the content of aromatic elements common for wood lignins is lower in cotton seed husks than in wood.

2. The composition of cotton seed husk lignin includes elements which contain the aromatic nuclei of syringic and guaiacyl structure.

No elements with hydroxyphenyl radicals were found in this lignin.

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Received December 30, 1956

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*In Russian.

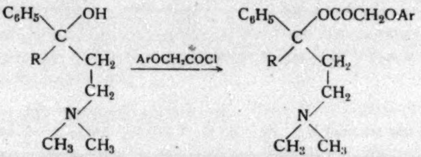
SYNTHETIC ANESTHETICS

XXII. PHENOXYACETATES OF 1-PHENYL-3-DIMETHYLAMINOPROPAN-1-OLS

I. N. Nazarov and E. M. Cherkasova

Previous papers [1,2] describe the preparation of a series of esters of 1-phenyl-3-dialkylaminopropan-1-ols and among them were found some compounds with a high anesthetic activity. Thus, for example, the phenoxyacetate of 1-phenyl-1-ethyl-3-dimethylaminopropan-1-ol was found to be a very strong anesthetic, as active as dicaine but considerably less toxic. In connection with this, it seemed interesting to synthesize a series of other phenoxyacetates of 1-phenyl-3-dialkylaminopropan-1-ols and to follow systematically the relation between the structure of these compounds and their physiological activity.

For this purpose we prepared some substituted phenoxyacetates of 1-phenyl-3-dimethylaminopropan-1-ol, containing various substituents in the benzene nucleus of the phenoxyacetate group.

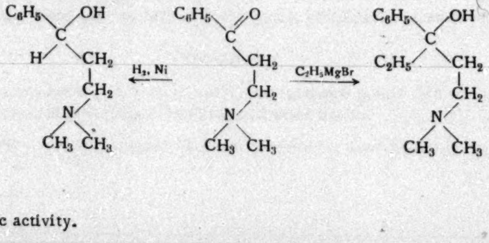


(I) (II)

$R = H, C_2H_5$; $Ar = C_6H_4CH_3$ (o-, m-, p-), $C_6H_4OCH_3$-p, $C_6H_4OC_2H_5$-p, $C_6H_3Cl_2$ (2,4)

In order to test the anesthetic effect, we also prepared the cinnamic ester of the amino alcohol (I, R=H) as in some other cases such esters were found to be valuable [1].• We attempted to reduce the p-nitrobenzoate of the amino alcohol (I, $R = C_2H_5$) with stannous chloride and hydrochloric acid to the corresponding p-aminobenzoate, but this reaction gave a very small yield. Attempts at catalytic reduction gave negative results.

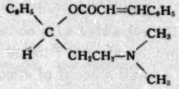
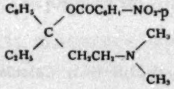
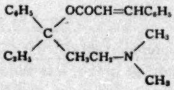
The starting amino alcohols (I) were prepared, as described previously [1], by the Mannich reaction from acetophenone and dimethylamine followed by reduction of the β-dimethylaminopropiophenone thus formed or treatment of it with a Grignard reagent:



• See table of anesthetic activity.

The esters (II) obtained were tested pharmacologically as the hydrochlorides in the laboratory of M. D. Mashkovskii and it was found that the cinnamic ester of 1-phenyl-3-dimethylaminopropan-1-ol and the p-nitrobenzoate and m-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol were active surface anesthetics. The p-cresoxyacetate and p-methoxyphenoxyacetate of the tertiary alcohol (I, R = C_2H_5) had activities approaching that of dicaine as their indexes in a 0.5% solution were 1200 and 1180 respectively (1300 for dicaine) but the activities of the solutions dropped sharply after sterilization. Thus, the introduction of a methyl or methoxyl group into the position para to the phenolic hydroxyl decreased the stability of the phenoxyacetates described, to hydrolysis. As could be expected, the 2,4-dichlorophenoxyacetate of the amino alcohol (I, R = C_2H_5) had a strong irritating effect: a 0.5% solution of it caused strong edema of the mucous membrane of a rabbit's eye and therefore, was not investigated in detail. The o-cresoxyacetate of the amino alcohol (I, R = C_2H_5) was not investigated for the same reason, while the p-ethoxyphenoxyacetate was insoluble in water. The results of the tests are summarized in the table.

The Anesthetic Activity of The Hydrochlorides of Phenoxyacetates (II) and Others

Formula of preparation	Index	
	anesthesia (0.5%)	after sterilization (0.5%)
Dicaine	1300*	1300
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_4CH_3\text{-}p \end{array} \right.$	1200	56.5
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_4OCH_3\text{-}p \end{array} \right.$	1180	22.5
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_3Cl_2(2,4) \end{array} \right.$	Has irritating effect	
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_4CH_3\text{-}o \end{array} \right.$	Has irritating effect	
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_4OC_2H_5\text{-}p \end{array} \right.$	Soluble in water only on heating	
(II) $\left\{ \begin{array}{l} R = C_2H_5 \\ Ar = C_6H_4CH_3\text{-}m \end{array} \right.$	951	
	354	
	413	
	1067** (0.25%)	Activity remained unchanged

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*Average fatal dose 8 mg/kg.

**Average fatal dose 35 mg/kg.

EXPERIMENTAL

The acid chlorides of the substituted phenoxyacetic acids were prepared in 80-90% yields by the action of thionyl chloride on the substituted phenoxyacetic acids, which were prepared in their turn from appropriate phenols and chloroacetic acid in the presence of alkali. As an example, the preparation of o-cresoxyacetyl chloride is described below.

10 g of freshly distilled thionyl chloride (b. p. 76-78°) was added with cooling to 5 g of o-cresoxyacetic acid (m. p. 150°) [3]. The next day the mixture was heated for 4 hours on a water bath at 60-80°, the excess thionyl chloride distilled off and the residue vacuum distilled. We obtained 4 g of o-cresoxyacetyl chloride with b. p. 108-110° (6 mm) [4].

1-Phenyl-3-dimethylaminopropan-1-ol (I, R = H). 6.3 g of β-dimethylaminopropiophenone hydrochloride [5] (m. p. 152-153°) in 60 ml of anhydrous alcohol was hydrogenated in the presence of 1 g of nickel catalyst. The hydrogenation lasted for 2.5 hours and 1090 ml of hydrogen was absorbed (against 724 ml, calculated theoretically). The catalyst was filtered off, the alcohol distilled off under reduced pressure and the residue twice recrystallized from acetone. We obtained 2.34 g of 1-phenyl-3-dimethylaminopropan-1-ol hydrochloride (I, R = H) with m. p. 132-133° [5].

Found %: N 6.53, 6.68. $C_{11}H_{17}ON \cdot HCl$. Calculated %: N 6.5.

Cinnamate of 1-phenyl-3-dimethylaminopropan-1-ol. 6.5 g of cinnamyl chloride (m. p. 35°) in 8 ml of benzene was added to a solution of 1.5 g of 1-phenyl-3-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. The mixture, which rapidly crystallized, was heated for 2 hours at the boiling point of the benzene. The next day the precipitated crystals were washed with absolute ether and treated with 25% ammonia. The liberated base was extracted with ether and dried with sodium sulfate. After distilling off the ether and the starting amino alcohol (b. p. 107° at 2 mm, hydrochloride, m. p. 130-132°, 0.6 g), we directly converted the residue into the hydrochloride in a chloroform solution. We obtained 1.05 g of the cinnamate of 1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 176-176.5°.

Found %: C 69.71, 69.60; H 6.82, 6.92; N 4.08, 3.95. $C_{20}H_{23}O_2N \cdot HCl$. Calculated %: C 69.45; H 6.94; N 4.05.

From the benzene mother liquors we isolated 0.9 g of the hydrochloride of the starting amino alcohol with m. p. 132-133°.

o-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-o). To a solution of 1.2 g of freshly distilled 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1] in 5 ml of anhydrous benzene was added 0.1 g of magnesium and then 2.5 g of freshly distilled o-cresoxyacetyl chloride (b. p. 106-107° at 6 mm) in 5 ml of anhydrous benzene gradually was added with cooling in ice water. The mixture was kept for 2 days at room temperature and then the precipitate was filtered off, washed with ether and recrystallized from anhydrous acetone with the addition of a small amount of ether until the acetone solution became turbid. We obtained 1.7 g of the o-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 146-148°.

Found %: C 67.02, 66.50; H 7.96, 7.96; N 3.37, 3.61. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

m-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-m). To 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], cooled in ice, was added 4 g of m-cresoxyacetyl chloride (b. p. 89-91° at 3 mm) [4]. The mixture was heated for 3 hours on a boiling water bath, after which anhydrous ether was added with cooling. The following day the precipitate obtained was filtered off, washed with ether and recrystallized 5 times from acetone. We obtained 0.62 g of the m-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 156-157°.

Found %: C 66.62; 66.82; H 7.75, 7.71; N 3.64, 3.68. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

p-Cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4CH_3$-p). 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 0.2 g of magnesium turnings, 5 g of p-cresoxyacetyl chloride (b. p. 85-88° at 3 mm) and 14 ml of anhydrous ether were used. The mixture was treated as in the previous experiment. We obtained 0.8 g of the p-cresoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 145-146° (from acetone).

Found %: C 67.18, 66.85; H 7.57, 7.58; N 3.95, 3.73. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 67.50; H 7.70; N 3.56.

p-Methoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4OCH_3$-p). 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1] and 4 g of freshly distilled p-methoxyphenoxyacetyl chloride (b. p. 121-123° at 3 mm) [6] were mixed and cooled in ice water. The mixture was heated for 4 hours on a boiling water bath and kept for several days at room temperature. The glassy mass precipitated was triturated several times with anhydrous ether (50 ml). The ether was poured off and the residue twice recrystallized from acetone. We obtained 0.23 g of p-methoxyphenoxyacetate hydrochloride with m. p. 148-149°. The acetone was distilled off from the mother liquors and the residue dissolved in 15 ml of anhydrous alcohol and boiled for 15 minutes with animal charcoal. The latter was filtered off, ether added until the alcohol solution became turbid and the precipitate recrystallized from acetone. We obtained a further 2.4 g of the p-methoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 147-148°.

Found %: N 3.63, 3.74. $C_{22}H_{29}O_4N \cdot HCl$. Calculated %: N 3.44.

p-Ethoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol (II, R = C_2H_5, Ar = $C_6H_4OC_2H_5$-p). 1.5 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 3.5 g of freshly distilled p-ethoxyphenoxyacetyl chloride (b. p. 120-125° at 3 mm) and 25 ml of a mixture of anhydrous acetone, benzene and ether (1 : 1 : 1) were used. The mixture was heated on a water bath for 1.5 hours. The following day the precipitated mass was triturated with ether and the residue separated off, washed with ether and recrystallized 4 times from acetone. We obtained 0.89 g of the p-ethoxyphenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 160-161°.

Found %: C 65.18, 65.49; H 7.87, 7.79; N 3.62, 3.52. $C_{23}H_{31}O_4N \cdot HCl$. Calculated %: C 65.48; H 7.53; N 3.32.

2,4-Dichlorophenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [II, R = C_2H_5, Ar = $C_6H_3Cl_2$ (2,4)]. 5.8 g of 2,4-dichlorophenoxyacetyl chloride (m. p. 45°) [7] in 10 ml of benzene was added to a solution of 2 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol in 5 ml of benzene, cooled in ice water. The mixture was heated for 4 hours at 80-85°. The following day the reaction mass was treated as described in the previous experiment. We obtained 1.93 g of the 2,4-dichlorophenoxyacetate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 159-160° (from acetone).

Found %: C 56.75, 56.65; H 6.18, 6.03; N 3.14, 3.23. $C_{21}H_{25}O_3NCl_2 \cdot HCl$. Calculated %: C 56.4; H 5.8; N 3.17.

p-Nitrobenzoate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol. 4 g of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol [1], 10.9 g of p-nitrobenzoyl chloride (m. p. 73°) [8] and 10 ml of chloroform were heated on a water bath at 70-75° for 2 hours. The following day the reaction mass was treated as described above. We obtained 3.6 g of the p-nitrobenzoate of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 157-158° (from anhydrous alcohol).

Found %: C 60.92; 60.88; H 6.73, 6.63; N 7.26, 7.27. $C_{20}H_{24}O_4N_2 \cdot HCl$. Calculated %: C 61.10; H 6.36; N 7.10.

SUMMARY

A series of substituted phenoxyacetates of 1-phenyl-3-dimethylaminopropan-1-ols, which are active local anesthetics, were synthesized. However, none of these esters were more interesting as anesthetics than the unsubstituted phenoxyacetates.

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Received December 14, 1956

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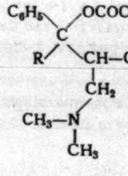
*Original Russian pagination. See C. B. Translation.

SYNTHETIC ANESTHETICS

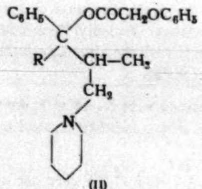
XXIII. PHENOXYACETATES OF 1-PHENYL-2-METHYL-3-DIALKYLAMINOPROPAN-1-OLS

I. N. Nazarov, E. M. Cherkasova and Ch'ang Ch'ung Kwang

As highly active anesthetics were found among the phenoxyacetates of 1-phenyl-3-dialkylaminopropan-1-ols [1], we synthesized a series of phenoxyacetates of 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols, represented by formulas (I) and (II), in order to elucidate the effect of the methyl group in the propanol chain on the physiological activity of these compounds.



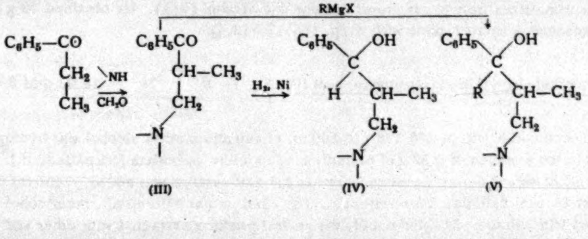
(I)



(II)

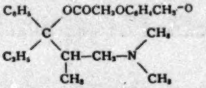
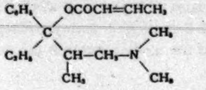
R=H, CH_3, C_2H_5, n.-C_3H_7, n.-C_4H_9, iso-C_5H_{11}.

Using other examples, the positive effect of such branching in the alkanolamine chain on the physiological (anesthetic) activity of the esters had been noted previously [2]. The starting 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols were prepared, as described previously [2], from propiophenone by the Mannich reaction. The amino ketones (III) thus formed were hydrolyzed to the corresponding secondary amino alcohols (IV) or were converted into tertiary amino alcohols (V) by treatment with Grignard reagents.



(III) (IV) (V)

Dimethylamine and piperidine were used as secondary amines in the Mannich reaction. The amino alcohols (IV) and (V) obtained, were converted into the corresponding phenoxyacetates by treatment with phenoxyacetyl chloride.

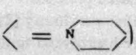
Formula of preparation	Anesthesia index				Anesthesia index after sterilization (0.25%)	Average fatal dose (in mg/kg)
	0.1%	0.25%	0.5%	1%		
Dicaine	947	1196	1300	1300		8.5
(II) $R = C_2H_5$	947	1300		1300	897	6.7
(II) $R = CH_3$	645	1146		1264	957	11
(I) $R = n\text{-}C_4H_9$		1300		1300	219	
		1300		1300	Precipitates	
			65			

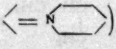
In addition, we prepared the p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol and the crotonic ester of this amino alcohol so as to compare it with the cinnamic ester of 1-ethyl-1-phenyl-3-dimethylaminopropan-1-ol, whose activity was extremely high [9].

Some of the esters synthesized were tested as hydrochlorides in a pharmacological laboratory for surface anesthesia and were found to be strong anesthetics, similiar in activity to dicaine. The results of the tests are summarized in the table.

The phenoxyacetates (II, R = H, n-C_4H_9) were not tested due to their insolubility in water. The p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol was not tested for the same reason.

EXPERIMENTAL

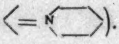
β-Piperidylisobutyrophenone (III, N ) A mixture of 40.2 g of propiophenon (b. p. 213-214°), 36.4 g of piperidine hydrochloride, 16 g of paraformaldehyde, 1 ml of concentrated hydrochloric acid and 100 ml of ethyl alcohol was heated for 8 hours on a boiling water bath. During this time a further 20 g of paraformaldehyde was added. The solvent was distilled off under reduced pressure and the residual mass recrystallized from a mixture of acetone and alcohol (5 : 1). We obtained 59 g (73%) of β-piperidylisobutyrophenone hydrochloride with m. p. 168-170° [3,4].

1-Phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (IV, N ). 16.05 g of β-piperidylisobutyrophenone hydrochloride (m. p. 168-178°) in 100 ml of anhydrous ethyl alcohol was hydrogenated with continuous shaking in the presence of 0.82 g of palladium on calcium carbonate (5% palladium). The hydrogenation lasted for 16 hours and during this time a further 1.6 g of catalyst was added. 1400 ml of hydrogen was absorbed against 1458 ml calculated theoretically. The catalyst was filtered off, the alcohol distilled off, the residue acidified with dilute hydrochloric acid, the neutral products extracted with ether and the aqueous layer treated with a saturated solution of sodium hydroxide and extracted several times with ether. The ether solution was dried with sodium sulfate and the residue after evaporation of the ether was vacuum distilled. We obtained 11.8 g (84%) of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with b. p. 134-136° (2 mm), m. p. 49-50.5°.

Found %: N 6.09, 6.07. $C_{15}H_{23}ON$. Calculated %: N 6.00.

The amino alcohol hydrochloride melted at 225-227° (from alcohol).

Found %: N 5.03, 4.98. $C_{15}H_{23}ON \cdot HCl$. Calculated %: N 5.19.

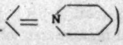
1,2-Dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (V, R = CH_3, N ).

With continuous stirring, 26.7 of β-piperidylisobutyrophenone hydrochloride was gradually added to an ether solution of methylmagnesium iodide, prepared from 47.4 g of methyl iodide, 7.2 g of magnesium and 130 ml of absolute ether, at a temperature of -12°. The following day the reaction mixture was acidified to Congo with dilute hydrochloric acid, the ether layer separated and the aqueous acid layer saturated with alkali and extracted several times with ether. The ether extract was dried with sodium sulfate. After vacuum distillation, the product crystallized (over 10 days). We obtained 19.2 g (77.5%) of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with m. p. 39-40° and b. p. 133-137° (1.5 mm).

Found %: N 5.65, 5.32. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The hydrochloride melted at 200-202° (from acetone).

Found %: N 5.26, 4.94. $C_{16}H_{25}ON \cdot HCl$. Calculated %: N 4.94.

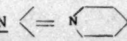
1-Ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = C_2H_5, N 

Under the conditions described above, 26.7 g of β-piperidylisobutyrophenone was added to the Grignard reagent prepared from 7.2 g of magnesium, 36.3 g of ethyl bromide and 100 ml of absolute ether. After working up the product as described in the previous experiment, we obtained 20.8 g (79.6%*) of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 64-65°.

Found %: C 78.35, 78.30; H 10.03, 10.15; N 5.01, 4.92. $C_{17}H_{27}ON$. Calculated %: C 78.20; H 10.07; N 5.30.

The hydrochloride had m. p. 210-212°.

Found %: N 4.77, 4.62. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.72.

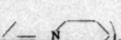
1-n-Propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = n-C_3H_7, N ).

26.7 g of β-piperidylisobutyrophenone hydrochloride was added to the Grignard reagent, prepared from 7.2 g of magnesium, 41 g of n-propyl bromide and 150 ml of absolute ether. After working the product up in the usual way, we obtained 13.6 g (50%) of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 58°.

Found %: C 78.56, 78.84; H 10.59, 10.20; N 5.16, 5.28. $C_{18}H_{29}ON$. Calculated %: C 78.5; N 10.5; H 5.1.

The hydrochloride melted at 185-186° (from acetone).

Found %: N 4.51, 4.66. $C_{18}H_{29}ON \cdot HCl$. Calculated %: N 4.50.

1-n-Butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = n-C_4H_9, N ).

26.7 g of β-piperidylisobutyrophenone hydrochloride was added to the Grignard reagent, prepared from 7.2 g of magnesium, 47.5 g of n-butyl bromide and 100 ml of anhydrous ether. After working up the product in the usual way, we obtained 20.7 g (71.5%) of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with m. p. 41-42°.

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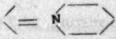
* This alcohol was prepared [5] in 26.5% yield and the hydrochloride had m. p. 216-218°.

Found %: N 4.89, 4.70. $C_{19}H_{31}ON$. Calculated %: N 4.84.

The hydrochloride melted at 155-156° (from acetone).

Found %: N 4.36, 4.18. $C_{19}H_{31}ON \cdot HCl$. Calculated %: N 4.30.

1-Isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (V, R = iso-C_5H_{11}, N ).

A Grignard reagent was prepared from 7.2 g of magnesium, 51 g of isoamyl bromide and 100 ml of absolute ether. In the usual way, 26.7 g of β-piperidylisobutyrophenone hydrochloride was added to it. The mixture was worked up as described above. We obtained 24.75 g (81.5%) of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol with b. p. 158-162° (2 mm).

Found %: N 4.49, 4.48. $C_{20}H_{33}ON$. Calculated %: N 4.62.

The hydrochloride melted at 170° (from acetone).

Found %: N 4.21, 3.97. $C_{20}H_{33}ON \cdot HCl$. Calculated %: N 4.12.

The phenoxyacetate of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = H). 5.25 g of phenoxyacetyl chloride (b. p. 102-104° at 9 mm) [6] was added dropwise, followed by 5 drops of sulfuric acid, to 46.6 g of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol in 30 ml of anhydrous ether at 0°. The mixture was left for 2 days and then heated for 1 hour at the boiling point of the ether. The precipitate was separated, washed with ether and triturated in the hot with anhydrous acetone. The insoluble residue was filtered off (2.68 g) and found to be the hydrochloride of the starting amino alcohol (m. p. 223°), which did not depress the melting point of an authentic sample.

Found %: N 5.19, 4.84. $C_{15}H_{23}ON \cdot HCl$. Calculated %: N 5.19.

A small amount of anhydrous ether was added to the acetone mother liquor and the precipitate recrystallized from acetone. We obtained 4.72 g (58.5%) of the phenoxyacetate of 1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 136-138°.

Found %: C 68.03, 67.90; H 7.31, 7.43; N 3.67, 3.73. $C_{23}H_{29}O_3N \cdot HCl$. Calculated %: C 68.3; H 7.43; N 3.47.

The phenoxyacetate of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (II, R = CH_3). The reaction mixture consisted of 4.94 g of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, 5.25 g of freshly distilled phenoxyacetyl chloride and 70 ml of absolute ether and was kept for 2 hours at 0° and then for 5 days at room temperature. The precipitate was filtered off, washed with ether 3 times and recrystallized from acetone 4 times. We obtained 7.06 g (84.5%) (from all the mother liquors we isolated 4.91 g of material by a second recrystallization) of the phenoxyacetate of 1,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 161-163°.

Found %: C 68.62, 69.01; H 7.74, 7.55; N 3.01, 3.30. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69.0; H 7.66; N 3.36.

The phenoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = C_2H_5). 5.25 g of phenoxyacetyl chloride in 20 ml of ether and 3 drops of concentrated sulfuric acid were added to a solution of 5.22 g of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol in 50 ml of absolute ether, cooled with ice water. The mixture was kept for a week. The ether layer was poured off and the crystalline residue (8.22 g) treated twice with absolute ether at 30° and dissolved in a mixture of chloroform and acetone by heating. On cooling, the solution deposited 0.87 g of the hydrochloride of the starting amino alcohol with m. p. 211-212°.

Found %: N 4.70, 4.61. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.72

Anhydrous ether was added to the mother liquor until the product completely precipitated and this was recrystallized from a mixture of chloroform and acetone. We obtained 2.77 g (32%) of the phenoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 162.5-163°.

Found %: C 69.41, 69.29; H 7.67, 7.44; N 3.41, 3.28. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.85; N 3.24.

The phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, n-C_3H_7). A mixture of 4.82 g of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 4 g of phenoxyacetyl chloride, 0.1 g of magnesium and 40 ml of absolute ether was kept for 2 days. The precipitate was washed with anhydrous ether until the smell of the acid chloride disappeared and then recrystallized from a mixture of chloroform and ether. We obtained 4.49 g (57%) of the phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 176-176.5°.

Found %: C 70.22, 69.91; H 8.91, 9.22; N 2.97, 3.22. $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 70.03; H 8.08; N 3.14.

The phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = n-C_4H_9). A mixture of 5.78 g of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 5 g of phenoxyacetyl chloride and 70 ml of ether was treated as described in the previous experiments, after standing for 2 days at room temperature. We obtained (after 3 recrystallizations from acetone) 4.35 g (47.5%) of the phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 163-165°.

Found %: C 70.59, 70.41; H 7.83, 8.02; N 3.15, 2.98. $C_{27}H_{37}O_3N \cdot HCl$. Calculated %: C 70.5; H 8.25; N 3.05.

The phenoxyacetate of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol (II, R = iso-C_5H_{11}). 6.06 g of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 5 g of phenoxyacetyl chloride and 70 ml of ether were used. After standing for 3 days at room temperature, the reaction product was treated as described above. Three recrystallization from acetone yielded 5.25 g (54%) of the phenoxyacetate of 1-isoamyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 140-140.5°.

Found %: C 71.01, 71.32; H 8.15, 7.94; N 3.15, 3.28. $C_{28}H_{39}O_3N \cdot HCl$. Calculated %: C 71.0; H 8.45; N 2.96.

The p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol. 3 g of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol [5], 7.5 g of p-nitrobenzoyl chloride and 20 ml of chloroform were heated at 50-60° for 3 hours. The precipitate was triturated with anhydrous ether and purified by 3 recrystallizations from alcohol. We obtained 3.2 g (60.5%) of the p-nitrobenzoate of 1-ethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol hydrochloride with m. p. 169-170°.

Found %: C 63.86, 63.79; H 6.66, 6.88; N 6.27, 6.39. $C_{23}H_{28}O_4N_2 \cdot HCl$. Calculated %: C 63.81; H 6.75; N 6.42.

The phenoxyacetate of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol (I, R = H). 3.4 g of freshly distilled phenoxyacetyl chloride (b. p. 109-110° at 13 mm) in 4 ml of benzene was added to a solution of 1.9 g of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2] (m. p. 87-89°) in 6 ml of anhydrous benzene, cooled in ice water. After 3 days, anhydrous ether was added and the mixture heated on a water bath for 0.5 hours. The precipitate was separated, washed 3 times with ether and purified by recrystallization from acetone. We obtained 2.3 g (64.5%) of the phenoxyacetate of 1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 154-156°.

Found %: C 66.53, 66.32; H 7.44, 6.97; N 3.93, 4.22. $C_{20}H_{25}O_3N \cdot HCl$. Calculated %: C 66.1; H 7.15; N 3.85.

The phenoxyacetate of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (I, R = CH_3). A mixture of 2.1 g of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol [2], 4.35 g of phenoxyacetyl chloride, 0.1 g of magnesium and 6 ml of benzene was kept for 24 hours and then worked up as described above. We obtained 2.5 g (65.2%) of the phenoxyacetate of 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 160-161° (from acetone).

Found %: C 66.36, 67.04; H 7.27, 7.55; N 3.38, 3.67. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: C 66.7; H 7.42; N 3.70.

The phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-dimethylamonopropan-1-ol (I, R = n-C_3H_7). From 2.4 g of 1-n-propyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 2.6 g of phenoxyacetyl chloride and 14 ml of a mixture of acetone and ether (7 : 3), using the procedure described above, we obtained 0.5 g (12.1%) of the phenoxyacetate of 1-n-propyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 153-155° (from acetone).

Found %: C 68.07, 68.46; H 7.51, 7.53; N 3.95, 3.70. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.10; H 7.90; N 3.46.

The phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol (I, R = n-C_4H_9). After being treated as described above, 2.5 g of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 4.65 g of phenoxyacetyl chloride, 0.1 g of magnesium and 6 ml of anhydrous benzene yielded 2.3 g (54.7%) of the phenoxyacetate of 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 172.5-174° (from acetone).

Found %: C 68.58, 68.13; H 8.05, 8.24; N 3.47, 3.32. $C_{24}H_{33}O_3N \cdot HCl$. Calculated %: C 68.7; H 8.11; N 3.34.

The o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol. From 2.2 g of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 3.35 g of o-cresoxyacetyl chloride [7], 0.1 g magnesium and 12 ml of anhydrous benzene by the usual method, we obtained 2.3 g (56%) of the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 157-158° (from acetone).

Found %: C 67.64, 68.32; H 7.69, 7.82; N 3.33, 3.43. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.1; H 7.90; N 3.46.

The crotonate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol. By the usual procedure, 3.32 g of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol [2], 3.3 g of crotonyl chloride (freshly distilled at 122-124°) [8] and 13 ml of anhydrous benzene yielded 1.5 g (30.6%) of the crotonate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol hydrochloride with m. p. 182-183° (from acetone).

Found %: C 66.16, 66.12; H 8.30, 8.34; N 4.10, 4.45. $C_{18}H_{27}O_2N \cdot HCl$. Calculated %: C 66.4; H 8.60; N 4.30.

SUMMARY

In order to test them pharmacologically, we synthesized a series of phenoxyacetates of 1-phenyl-2-methyl-3-dialkylaminopropan-1-ols and some of the compounds had an anesthetic activity as strong as that of dicaine (phenoxyacetates of 1-ethyl-1-phenyl-2-methyl-3-(N-piperidyl)-propan-1-ol, 1,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 1-n-butyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol and the o-cresoxyacetate of 1-ethyl-1-phenyl-2-methyl-3-dimethylaminopropan-1-ol).

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Received December 14, 1956

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*Original Russian pagination. See C. B. Translation.

OXIDATION OF ORGANIC COMPOUNDS

XV. VAPOR PHASE OXIDATION OF ETHYLBENZENE ON TIN VANADATE

A. V. Solomin, B. V. Suvorov and S. R. Rafikov

The catalytic vapor phase oxidation of alkylbenzenes with a secondary α-carbon atom has been little studied. There is only one paper on this problem [1] and it reports that passing a mixture of ethylbenzene vapor and air gave only benzoic acid. At 270-280° the yield was 41%. The purpose of this work was to study thoroughly the basic rules governing this reaction. The intermediate and final reaction products in the oxidation of ethylbenzene were especially carefully studied. Some of the intermediate compounds were oxidized under comparable conditions.

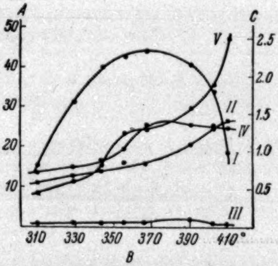
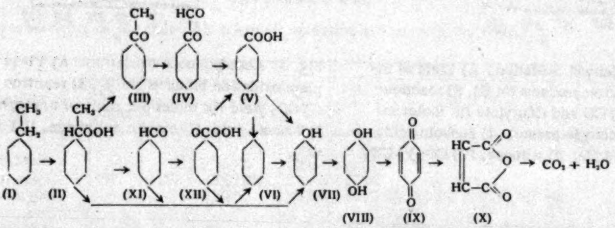


Fig. 1. Ethylbenzene oxidation. A) Yield of products of incomplete oxidation (in %). B) reaction temperature, C) CO and CO_2 yield (in moles per mole of ethylbenzene passed). I) Benzoic acid, II) maleic anhydride, III) quinone, IV) CO, V) CO_2.

The experimental data obtained showed that vapor phase oxidation of ethylbenzene with atmospheric oxygen in the presence of tin vanadate was a complex process and, depending on the conditions, formed widely differing oxygen-containing compounds. Thus, besides benzoic acid, we isolated and determined quantitatively benzaldehyde, acetophenone, quinone, maleic anhydride, CO and CO_2. The relation of the yields of some of these reaction products to temperature is shown in Fig. 1. This figure shows that there is a definite sequence in the distribution of the maxima of the yield curves of the main products of incomplete oxidation. Characteristically, the greatest amounts of quinone were formed in the temperature range at which benzoic acid yield started to decrease. A further rise in temperature was conducive to maleic anhydride formation, but then the yield of quinone and particularly that of benzoic acid fell sharply. These facts seem to indicate that in ethylbenzene oxidation, a large part of the maleic anhydride was formed from benzoic acid through the intermediate formation of quinone. This hypothesis was confirmed by the formation of quinone and maleic anhydride in the oxidation of pure benzoic acid. However, the same experiments showed that in ethylbenzene oxidation, small amounts of quinone and maleic anhydride formed also at relatively low temperatures, at which benzoic acid is stable. This indicated that two simultaneous and parallel processes for their formation were possible and these omitted the benzoic acid stage. The mechanisms for the formation of the basic products of incomplete oxidation given here were also observed in experiments with benzaldehyde, acetophenone and phenylglyoxal. In ethylbenzene oxidation, the stages of benzaldehyde and acetophenone formation, without doubt, preceded the formation of benzoic acid, but occurred parallel to each other. The only other modification possible here – the conversion of acetophenone into benzaldehyde – was not confirmed experimentally.

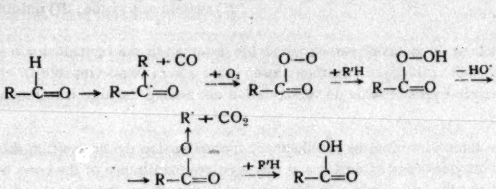
In the experiments investigated, besides the main reaction products, other oxygen-containing compounds were formed, among them phenol and peroxides. Although, only traces of these were found, their formation should also be considered as due to the existence of definite intermediate stages in the process of ethylbenzene oxidation. In connection with this, the peroxide compounds should be investigated thoroughly. We detected them only in ethylbenzene oxidation experiments carried out at a relatively low temperature.

However, the papers by K. I. Ivanov [2], V. Ia. Shtern [3] and other investigators, which prove the possibility of the formation of peroxide compounds during the oxidation of various hydrocarbons over an extremely wide temperature range, indicate that in a given case they also formed in other experiments at a higher reaction temperature. Such an assumption is of great value as it is then possible to consider the mechanism of the oxidation processes of ethylbenzene in the light of contemporary ideas on the peroxide theory of oxidation and theory of radical-chain processes. The scheme given for the main directions of ethylbenzene oxidation takes into consideration these data and explains quite well all the reaction mechanisms noted above.



The formation of ethylbenzene hydroperoxide (II) should be considered as the initial stage of the process. The subsequent stages are determined by the direction of the decomposition of this hydroperoxide. According to literature data [4], secondary unsymmetrical hydroperoxides may decompose in three directions. When the hydroperoxide (II) decomposes with the elimination of a water molecule, the subsequent intermediate reaction product would be acetophenone (III). When this is oxidized, it gives first phenylglyoxal (IV) and then benzoic acid (V). The benzoic acid is first decarboxylated. The phenyl radical thus formed may give benzene (VI) or may possibly react directly with oxygen. In both cases the reaction results in the formation of maleic anhydride (X). The intermediate products at this stage are, as we showed previously [5], phenol (VII), hydroquinone (VIII) and quinone (IX).

Another possible direction of decomposition of ethylbenzene hydroperoxide is characterized by the elimination of a methyl alcohol molecule to form benzaldehyde (XI). Liquid phase oxidation of benzaldehyde, as is known [6], proceeds through the intermediate stage of benzoyl hydroperoxide and ends with benzoic acid formation. This reaction sequence also occurs in benzaldehyde gas phase oxidation. However, in this case, due to the relatively large intramolecular distances and drastic temperature conditions, the monomolecular decarbonylation of benzaldehyde and decarboxylation of its hydroperoxide (XII) acquired considerable importance. From the point of view of radical-chain processes, these reactions may be written in the following way:



$$R-\overset{H}{C}=O \rightarrow R-\overset{\overset{R+CO}{\uparrow}}{\dot{C}}=O \xrightarrow{+O_2} R-\overset{O-O}{C}=O \xrightarrow{+R'H} R-\overset{O-OH}{C}=O \xrightarrow{-HO^{\cdot}}$$

$$\rightarrow R-\overset{\overset{\overset{R^{\cdot}+CO_2}{\uparrow}}{O}}{C}=O \xrightarrow{+P'H} R-\overset{OH}{C}=O$$

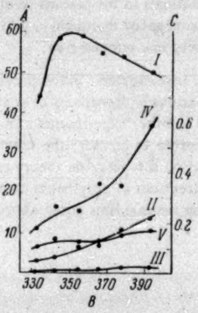


Fig. 2. Benzaldehyde oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO and CO_2 yield (in moles per mole of benzaldehyde passed). I) Benzoic acid, II) maleic anhydride, II) quinone, IV) CO, V) CO_2.

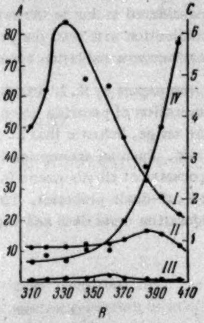


Fig. 3. Acetophenone oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO_2 yield (in moles per mole of acetophenone passed). I) Benzoic acid, II) maleic anhydride, III) quinone, IV) CO_2.

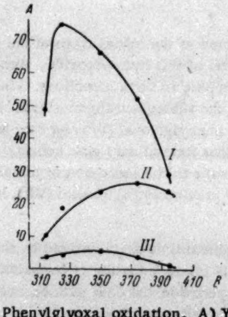


Fig. 4. Phenylglyoxal oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature. I) Benzoic acid, II) maleic anhydride, III) quinone.

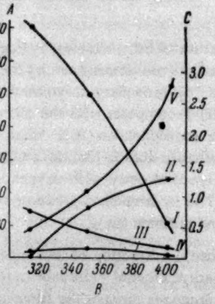


Fig. 5. Benzoic acid oxidation. A) Yield of incomplete oxidation products (in %), B) reaction temperature, C) CO and CO_2 yield (in moles per mole of benzoic acid passed). I) Unreacted benzoic acid (in %), II) maleic anhydride, III) quinone, IV) CO, V) CO_2.

The relatively large amounts of carbon monoxide detected in the benzaldehyde and ethylbenzene experiments indicate that benzaldehyde decarbonylation plays a very important role in ethylbenzene oxidation. Both it and benzaldehyde hydroperoxide decarboxylation are among the side reactions which hinder benzoic acid formation.

The last of the three directions of ethylbenzene hydroperoxide decomposition should also be examined as a side reaction in ethylbenzene oxidation and this involves the rupture of the bond between the carbon atoms of the aromatic ring and the side chain. In this case, as in the others, the phenyl radical is finally converted to maleic anhydride.

The scheme of the process was also confirmed by the analytical data on the gaseous reaction products. Figs. 1 and 2-5 show that in all the experiments carried out at temperatures below 350-370°, the products of incomplete ethylbenzene oxidation were mainly formed. However, the amount of complete oxidation products produced corresponded almost exactly (calculated on the CO_2) to the scheme:

$$\text{Ethylbenzene} \xrightarrow{-CO_2} \text{Benzoic acid} \xrightarrow{-CO_2} \text{Quinone} \xrightarrow{-2CO_2} \text{Maleic anhydride.}$$

Such a mechanism is quite natural as in this series of substances, maleic anhydride is the only compound which gives only an end reaction product when oxidized [5] and is quite stable under the given conditions. With rising temperature, the stability of the incomplete oxidation products decreased and they were converted more rapidly in all the stages and even the maleic anhydride was oxidized. In fact, at a temperature of 350-390°, the yield of incomplete oxidation products decreased as a rule and, at the same time, considerable evolution of CO and CO_2 began. Extensive oxidation became the predominating process above 390-410°.

EXPERIMENTAL

The characteristics of the materials taken for oxidation are given in the table.

Oxidizable material	Melting point	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Comments
Ethylbenzene	—	133.5° (697)	1.4954	0.8663	—
Acetophenone	19°	199.5—200 (704)	1.5340	1.0250	—
Benzaldehyde	—	176 (700)	1.5459	1.0511	Contained 3.1% of benzoic acid
Phenylglyoxal	87—88	—	—	—	Contained 6.5% of benzoylformic acid
Benzoic acid	121	—	—	—	Neutralization equivalent, 121.1

The oxidation of ethylbenzene and the other compounds was carried out in an all-metal reactor of the flow type, with a stainless steel reaction tube, 1100 mm long and 20 mm in diameter, heated with an electric furnace. The apparatus for the steady input of the starting materials into the reaction chamber and the system of trapping the solid reaction products were described in our previous papers [7, 8]. Granulated tin vanadate, in the form of grains 3-5 mm across, was used as the catalyst. Moist air, with a water content of 350 g/m³, was used as the oxidant. The experiments were performed with a contact time of 0.3-0.4 sec., the starting product input rate was 5-6 g/hour and the ratio of oxidizable material to air was 1:65 – 1:75. Only the reaction temperature was varied. The solid and liquid reaction products were identified and determined quantitatively by the methods described in previous papers [5, 9, 10]. The composition of the gaseous reaction products was determined using a VTI (All-Union Heat Engineering Institute) apparatus; the CO_2 determination was duplicated by absorbing it in barium hydroxide solution and the CO was determined in parallel by the hopcalite method [11].

Oxidation of ethylbenzene. Eight experiments were performed at temperatures from 310-410°. The temperature dependence of the main reaction products is shown in Fig. 1. At temperatures of 310-355°, benzaldehyde and acetophenone were detected among the reaction products. The yield of neither of these exceeded 2-3%. In all cases, qualitative reactions proved the presence of phenol, hydroquinone and formaldehyde. In two experiments carried out at 270-280° with freezing of the reaction products, the formation of peroxide compounds was demonstrated qualitatively.

Oxidation of benzaldehyde. The yields of the main products at different temperatures are shown in Fig. 2. In addition, we found 2.5 and 1% (respectively) of unreacted starting material in the first two experiments of this series. Qualitative reactions demonstrated the presence of phenol, hydroquinone and formaldehyde.

Oxidation of acetophenone. The yields of the main reaction products at different temperatures are shown in Fig. 3. In comparison with the other oxidized materials, acetophenone gave the greatest quantity of benzoic acid. At 332°, the yield of the latter was 85%. Among the oxidation products, we found phenol, hydroquinone and formaldehyde in all the experiments. Benzaldehyde was not found.

Oxidation of phenylglyoxal.* This compound was not found in the oxidation of ethylbenzene, despite the fact that it was considered as one of the probable intermediates of this reaction. As with acetophenone, phenylglyoxal was found to be extremely oxidizable. It reacted completely even at 320° (Fig. 4), when the maximum total yield of products of incomplete oxidation was 97%. Qualitative reactions for phenol, hydroquinone and formaldehyde were positive in all the experiments. Benzaldehyde was not found among the oxidation products. The CO and CO_2 were not determined.

Oxidation of benzoic acid. The products of incomplete oxidation in this case were phenol, quinone, maleic anhydride and CO and of these phenol was determined only qualitatively. At 350° about 50% of unreacted benzoic acid passed through the reaction chamber (Fig. 5) and this indicates its relatively high stability. To find the benzene in the products of benzoic acid oxidation, we carried out special experiments, in which the emergent gases were first frozen with liquid air and then passed through traps with activated charcoal and silica gel. Benzene could not be found by this method.

SUMMARY

1. We studied the vapor phase oxidation of ethylbenzene with moist air in the presence of tin vanadate. The oxidation of the intermediate products of this reaction was studied under comparable conditions.

2. A scheme for the main directions of the vapor phase oxidation of ethylbenzene over tin vanadate was put forward based on data from the peroxide theory of oxidation and the theory of radical-chain processes.

3. A hypothesis was put forward that ethylbenzene oxidation may proceed simultaneously in several parallel directions, both main and side processes. Each one of them is a multistage process of gradual destruction of the initial substances' carbon skeleton followed by the formation of numerous intermediate products. The final stage of each process is the formation of the products of complete oxidation.

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Received December 3, 1956

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*Prepared by the method described by Riley and Gray [12].

**In Russian.

SYNTHESIS, PROPERTIES AND POLYMERIZATION OF α-CHLOROACRYLAMIDE

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The amides of some acids of the acryl series may be prepared by a general method: by treating the appropriate esters with aqueous ammonia. Using this method, Arcus [1] prepared methacrylamide in good yield by shaking methyl methacrylate with excess concentrated ammonia in the cold.

α-Chloroacrylamide could not be synthesized by this method as, besides the substitution of the methoxyl group by the amide group, chlorine was eliminated. The authors of a French patent [2] report that α-chloroacrylamide may be prepared by hydrolyzing α-chloroacrylonitrile with sulfuric acid. However, this patent does not describe the method of isolating the α-chloroacrylamide from the reaction mixture and ways of purifying it and the characteristics given for the monomer itself are quite insufficient (only its m. p. of 93° is given).

We prepared α-chloroacrylamide in the same way by hydrolyzing α-chloroacrylonitrile (I) with sulfuric acid, in order to study its capacity for polymerization.

$$\underset{(I)}{CH_2{=}CCl{-}CN} \xrightarrow[H_2SO_4]{HOH} \underset{(II)}{CH_2{=}CClCONH_2}$$

The α-chloroacrylonitrile (I) was synthesized by dehydrochlorinating α, β-dichloropropionitrile with sodium acetate [3] and the α, β-dichloropropionitrile by chlorinating acrylonitrile in the presence of pyridine [3].

EXPERIMENTAL

Synthesis of α, β-dichloropropionitrile. Chlorine was passed into 53 g of acrylonitrile with 14 g of pyridine, cooled with water, for 3 hours until the reaction mixture had increased in weight by 71 g. The reaction product was shaken with distilled water in a separating funnel, dried with calcium chloride and distilled in vacuum at 61° (13 mm). We obtained 117.8 g (95%) of α, β-dichloropropionitrile as a colorless, lachrimatory liquid with a sharp smell, which was soluble in benzene, alcohol, dioxane and chloroform: d_4^{20} 1.338, n_D^{20} 1.4645 [3].

Found %: C 29.01; H 2.67; N 11.28; Cl 57.17. $C_3H_3NCl_2$. Calculated %: C 29.05; H 2.44; N 11.30; Cl 57.22.

Synthesis of α-chloroacrylonitrile (I). 56 grams of α, β-dichloropropionitrile, 50 ml of methyl alcohol and 60 g of sodium acetate were placed in a flask with a reflux condenser. The mixture was heated for 2 hours at 65°, washed with distilled water and the precipitated oil separated and dried with calcium chloride. Distillation on a column with copper packing in the presence of hydroquinone at atmospheric pressure gave 26.5 g (67%) of α-chloroacrylonitrile.

B. p. 87° (755 mm), 73° (726 mm), d_4^{20} 1.06, n_D^{20} 1.4301 [3].

The α-chloroacrylonitrile was a colorless, lachrimatory liquid with a sharp smell, which was soluble in benzene, dioxane, ether and chloroform.

Found %: C 41.03; H 2.42; N 15.92; Cl 40.47. C_3H_2NCl. Calculated %: C 41.15; H 2.30; N 16.01; Cl 40.57.

Synthesis of α-chloroacrylamide (II). 25.0 g of α-chloroacrylonitrile, 56.6 g of 85% sulfuric acid and 0.1 g of hydroquinone were placed in a 150 ml, thick-walled pyrex flask, fitted with a stirrer. The reaction mixture was stirred for 2 hours at 0°, 20 hours at 25°, 12 hours at 40° and 2 hours at 60° and then neutralized with a saturated solution of sodium bicarbonate after cooling in ice. The precipitated sodium sulfate crystals were separated and extracted 3 times with ether in portions of 100 ml each. The neutralized reaction mixture, whose volume usually did not exceed 350-500 ml, was shaken with equal volumes of ether until the α-chloroacrylamide was completely extracted, The ether extracts were combined and the ether evaporated off at room temperature in vacuum.

TABLE 1

Solubility of α-Chloroacrylamide at 20°*

Solvent	α-Chloroacrylamide (g) dissolved in 100 ml solvent
Acetone	94.70
Methanol	72.68
Ethanol	31.11
Ether	18.82
Chloroform	7.29
Carbon tetrachloride	7.26
Water	6.50
Benzene	3.76
Toluene	2.68

We obtained 18.5 g (61.4%) of α-chloroacrylamide with m. p. 90-94°. After recrystallization from benzene twice to remove traces of hydroquinone, the crystals of α-chloroacrylamide appeared as white plates with m. p. 94°. They decolorized a solution of bromine in acetic acid on heating, did not give a reaction for chlorine with $AgNO_3$ and gave off ammonia on boiling with concentrated alkali.

Found %: C 34.19; H 3.90; N 13.27; Cl 33.80. M (cryoscopic) 104.5; MR 22.48. C_3H_4ONCl. Calculated %: C 34.12; H 3.79; N 13.27; Cl 33.60. M 105.5; MR 23.06.

The crystals of α-chloroacrylamide were not very stable and on long storage (for more than a month) under normal conditions, they gradually decomposed with the loss of chlorine and nitrogen and a decrease in solubility and showed a double molecular weight in cryoscopic determinations. If solutions of α-chloroacrylamide fell onto the skin, they produced burns and blisters appeared.

At room temperature, α-chloroacrylamide was readily soluble in water, methyl and ethyl alcohols, acetone and ether and less soluble in benzene and toluene. Data on the solubility of α-chloroacrylamide is given in Table 1.

Bromination. The bromination of α-chloroacrylamide at room temperature occurred to a very small degree, even on keeping the reaction mixture in the dark for several days. On heating the material with a considerable excess of bromide – bromate mixture, the bromination went to completion.

The action of concentrated aqueous ammonia on α-chloroacrylamide. 1.0386 g of α-chloroacrylamide, dissolved in 100 ml of concentrated ammonia, was left to stand at room temperature for 7 days. The excess ammonia was evaporated off at room temperature in vacuum, when crystals of ammonium chloride were deposited (0.5032 g, 96.5%) and these were collected on a Schott filter.

Found %: Cl 66.26. NH_4Cl. Calculated %: Cl 66.30.

Traces of ammonium chloride were removed by several solutions in water and precipitations with methanol (test with $AgNO_3$).

An attempt to isolate the amide of pyruvic acid (m. p. 124-125°) by extraction of the tarry precipitate formed with chloroform and hot benzene [5] gave negative results. After drying in vacuum at room temperature , the tarry precipitate formed a clear, friable film of polymer, which was brown in color and had strong adhesion to glass. The polymer was readily soluble in water and was precipitated by methyl alcohol.

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* The solubility of α-chloroacrylamide was determined by the method described by Meier [4].

Found %: C 41.17; H 5.61; N 15.75. M 528. $(C_3H_5O_2N)_n$. Calculated %: C 41.38; H 5.75; N 16.10. M 87 (n = 6).

Polymerization of α-chloroacrylamide proceeded in block (in an atmosphere of air or nitrogen) in benzene solution in the presence of benzoyl peroxide and azoisobutyrodinitrile (0.2%) and also in an aqueous solution with hydrogen peroxide[1] and with potassium persulfate (0.02 mole%). The samples of block polymers, which were brown in color, were carefully powdered and washed with benzene and ether to remove monomer and initiator and then with distilled water until the Cl' was completely removed (reaction with $AgNO_3$).

The polymers obtained in benzene were treated as described above, after removal of the solvent, and after drying they formed white powders. These polymers were insoluble in water and the usual organic solvents (alcohols, acetone, ether, benzene, chloroform, dioxane, carbon tetrachloride, ethyl acetate, nitrobenzene and ammonia) both in the cold and on heating. In both cases the aqueous solutions, after washing the polymers, yielded variable amounts of ammonium chloride (from 3.3 to 8.8%), equivalent to the nitrogen liberated from the polymers. The polymerization in aqueous solutions with hydrogen peroxide and potassium persulfate began after several minutes at room temperature with the formation of a flocculent polymer. The addition of methanol to the aqueous solutions gave brown polymers which were readily soluble in water, slightly soluble in hot dimethylformamide and completely insoluble in the usual organic solvents and also pyridine, aniline, acetic anhydride and concentrated sulfuric acid. They swelled in hot nitrobenzene and in this state they could be formed into fibers and films [2]. On heating above 200° for 10 hours, the polymers lost their solubility in water, cross-linking like other thermosetting polymers. Data on the polymerization of α-chloroacrylamide is given in Table 2.

DISCUSSION OF RESULTS

On polymerizing α-chloroacrylamide we observed a noticeable decrease in the chlorine content and, to a lesser degree, in the nitrogen content of the polymers as compared with the content of the initial monomer; certain differences in the polymer composition were due to the nature of the polymerization initiators used (Table 2). Apparently, the elimination of chlorine and nitrogen cannot be explained by the thermal instability of the monomer as when α-chloroacrylamide was heated above its melting point (93-94°) there was resinification only in the temperature range 135-170°.

TABLE 2

α-Chloroacrylamide Polymerization

Polymerization conditions	Initiator	Time (hrs)	Temperature	Yield (%)	Content (%)	
					N	Cl
In block •	Benzoyl peroxide	36	100°	76.4	11.8	16.2
In block •	Azoisobutyrodinitrile	18	100	90.0	11.2	23.2
In block••	Benzoyl peroxide	24	100	70.5	10.2	18.3
In block••	Azoisobutyrodinitrile	18	100	76.0	11.3	23.8
In a solution of C_6H_6	Benzoyl peroxide	18	60	96.1	12.5	23.9
In a solution of C_6H_6	Azoisobutyrodinitrile	18	60	91.7	11.3	31.0
In a solution of H_2O•••	H_2O_2	18	60	84.5	6.5	3.8
In a solution of H_2O•••	$K_2S_2O_8$	—	—	98.7	2.6	1.8
Pyrolysis product••••	—	10	200	—	4.5	0.1
α-Chloroacrylamide	—	—	—	—	13.27	33.65

•In air.

••In an atmosphere of nitrogen.

•••Molecular weight (cryoscopic): 290.3 (with H_2O_2) and 400.0 (with $K_2S_2O_8$).

••••Polymer, obtained from H_2O_2.

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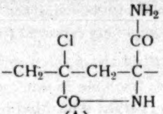
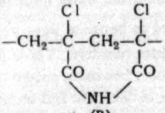
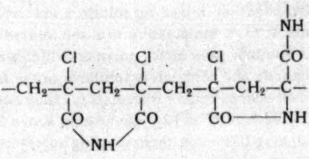
[1] Into the ampule was placed several drops of concentrated aqueous ammonia.

The liberation of ammonium chloride in α-chloroacrylamide polymerization indicated the existence of secondary reactions proceeding during the polymerization and accompanied by the elimination of chlorine (in the form of HCl) and nitrogen (in the form of NH_3). Apparently, at the same time both in block and in a benzene solution cyclic polymer units of the type (A) and (B) are formed and due to secondary reactions they form cellular (cross-linked), insoluble structures of type (C).


(A)


(B)


(C)

In aqueous solutions α-chloroacrylamide polymerized with the substitution of chlorine by hydroxyl from the water and partial hydrolysis of the amide group, catalyzed by the hydrogen chloride evolved. Heating such water soluble polymers above 200° resulted in the elimination of the elements of water to give cross-linked polymers.

SUMMARY

1. We describe a method of synthesizing, isolating and purifying α-chloroacrylamide.

2. Some of the properties of α-chloroacrylamide and its polymer were characterized.

3. It was shown that treatment of α-chloroacrylamide with concentrated aqueous ammonia at room temperature resulted in chlorine elimination and the formation of a polymer of low molecular weight.

4. It was shown that α-chloroacrylamide polymerization proceeded with nitrogen and chlorine elimination to form cross-linked polymers in block or in a benzene solution. In an aqueous solution, a partially hydrolyzed poly-α-hydroxyacrylamide was formed, which was soluble in water.

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Received January 2, 1957

A STUDY OF THE CHEMICAL STRUCTURE OF THE SPONGY DIVINYL POLYMER. II.

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We had previously [1] established that the ozonolysis products of spongy divinyl polymer contained formic, succinic, butane-1,2,4-tricarboxylic and hexane-1,x,y,6-tetracarboxylic acids.* This indicated that the spongy divinyl polymer contained the same sections as were found in the ozonolysis products of divinyl caoutchoucs, prepared under various conditions [2], namely: 1) formed by units with an internal double bond which was repeated at least 2 times in succession, 2) sections in which a unit with an external double bond was enclosed by units with an internal double bond, and 3) sections in which 2 units with an external double bond were enclosed by units with an internal double bond.** Kahrach [3] put forward the hypothesis that this polymer was a cross-linked polymer. As we found no substances in the ozonolysis products of the spongy polymer which would have indicated a steric structure, in this work we investigated more fully the ozonolysis products of the spongy divinyl polymer, changing the conditions under which they were isolated. In the previous work [1] the acid ozonolysis products were converted to methyl esters, which were separated by fractional distillation.

In the present work we separated the acids by partition chromatography which made it possible to separate the acids more precisely, as they differed very little in structure and molecular weight, and to detect them, even if they were in minute quantities.

The decomposition products of the ozonide of the spongy divinyl polymer contained, besides succinic, butane-1,2,4-tricarboxylic and hexane-1,x,y,6-tetracarboxylic acids, propane-1,2,3-tricarboxylic and levulinic acids. Also, it can be assumed that peak II on chromatogram 1 (Fig. 1) corresponded to propionic acid.***

The propionic acid could have been formed from the section -1,4-1,4- by anomalous ozonolysis. Propane-1,2,3-tricarboxylic acid could have been formed during the oxonolysis of the branched or cross-linked section formed in the transfer of the chain by the α-methylene group in the -1,4-1,4- section. Marvel [5] put forward the hypothesis that the propane-1,2,3-tricarboxylic acid could be the anomalous product of the ozonolysis of sections -1,4-1,2-1,4-, or could be formed from the section -1,4-1,4- at the branching at the α-methylene groups, as the spongy divinyl polymer has a considerable number of α-methylene groups.

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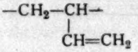
* The ozonolysis products may contain three isomeric hexanetetracarboxylic acids: hexane-1,2,4,6-tetracarboxylic, hexane-1,3,5,6-tetracarboxylic and hexane-1,2,5,6-tetracarboyxlic acids [4], formed from the sections: 1,4-1,2-1,2-1,4-, -1,4-1,2-2,1-1,4-,-1,4-2,1-1,2-1,4.

** Units, formed by adding divinyl at the 1,4-position are called units with an internal double bond (I) and those formed by addition at the 1,2 position – units with an external double bond (II).

$-CH_2-CH=CH-CH_2-$

(I)



$$-CH_2-CH(-CH=CH_2)-$$

(II)

*** As shown by work carried out in our laboratory.

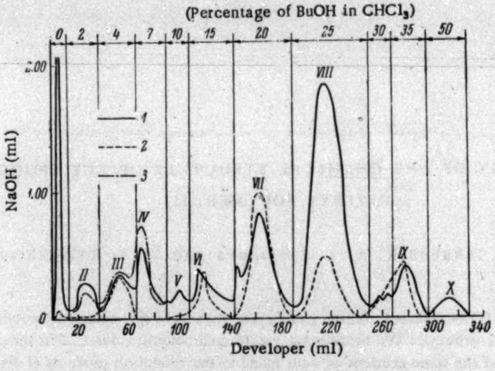
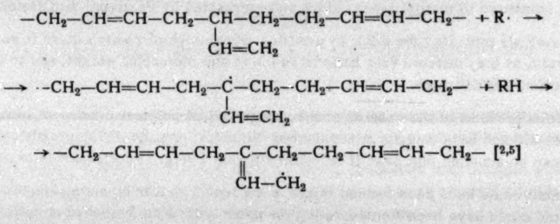


Fig. 1. 1) Partition chromatogram of liquid acids, 2) partition chromatogram of standard acid mixture, 3) partition chromatogram of liquid acids with levulinic and acetic acids added. Explanation in the text.

The levulinic acid could have been formed by the scheme



$$\mathrm{-CH_2-CH=CH-CH_2-\underset{\substack{|\\ CH=CH_2}}{CH}-CH_2-CH_2-CH=CH-CH_2-} + \mathrm{R}\cdot \rightarrow$$

$$\rightarrow \mathrm{-CH_2-CH=CH-CH_2-\underset{\substack{|\\ CH=CH_2}}{\dot{C}}-CH_2-CH_2-CH=CH-CH_2-} + \mathrm{RH} \rightarrow$$

$$\rightarrow \mathrm{-CH_2-CH=CH-CH_2-\underset{\substack{\|\\ CH-\dot{C}H_2}}{C}-CH_2-CH_2-CH=CH-CH_2-}\ [2,5]$$

Figures 1 and 2 show the chromatograms obtained by the separation of the acids isolated from the ozonolysis products of the spongy divinyl polymer. We calculated from the chromatograms the percentage of polymer carbon skeleton in the acids and in the sections. The calculation results are given in Tables 1 and 2.

The oxidative decomposition products of the ozonide of the spongy divinyl polymer contained 74.4% of the carbon skeleton of the ozonized polyer. Of it, 68.7% was in the acids identified (see Fig. 1, peaks II, III, VII, VIII, IX, X; Fig. 2, peaks III, V, VI, VII) and 5.6% of the polymer carbon skeleton was in the acids of undetermined structure, which corresponded to peaks I and V in chromatogram 1 (Fig. 1). Besides that, chromatogram 1 had peaks which corresponded to acetic and formic acids.

Sections were found in the spongy divinyl polymer, which has no caoutchouc-like properties, that had the same structure as in divinyl caoutchoucs. As the properties of compounds with high molecular weight are determined not only by the chemical structure but also by the shape and size of the molecules and their relative position and interaction, it is possible that the spongy divinyl polymer consists of linear macromolecules, joined in bunches by an insoluble nucleus. The presence of a primer, introduced preliminarily or formed during polymerization, is a prerequisite condition for the formation of a divinyl autopolymer [6, 7].

TABLE 1

Name of acid	Percentage of polymer carbon skeleton in the acid
Propionic	1.00
Levulinic	4.93
Succinic	39.74
Butane-1,2,4-tricarboxylic	14.96
Propane-1,2,3-tricarboxylic	1.83
Hexane-1,x,y,6-tetracarboxylic	1.18

TABLE 2

Name of acid	Structure of polymer section	Polymer carbon skeleton in section (%)	Percentage	
			1,4	1,2
Propionic	—1,4—1,4—	1.00	1.00	—
Levulinic	—1,4—1,2—1,4—	7.89	3.95	3.95
Succinic	—1,4—1,4—	39.74	39.74	—
Butane-1,2,4-tricarboxylic	—1,4—1,2—1,4—	17.10	8.55	8.55
Propane-1,2,3-tricarboxylic	—1,4—1,4—	1.83	1.83	—
Hexane-1,x,y,6-tetracarboxylic	—1,4—(—1,2—)$_2$— —1,4—	1.18	0.39	0.78
		68.74	55.46	13.28

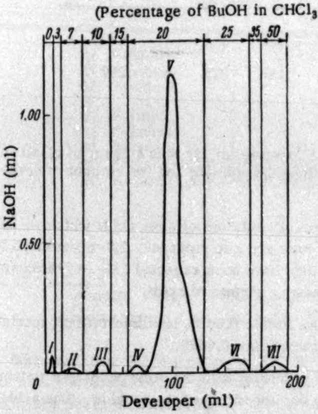


Fig. 2. Partition chromatogram of crystalline acids. Explanation in the text.

EXPERIMENTAL

The spongy polymer of divinyl was isolated from the autopolymer of divinyl, which was prepared by the slow polymerization of divinyl at 15-20° over a period of two years. The autopolymer of divinyl was readily oxidized in air and therefore all the work on the separation of the divinyl dimer and the soluble divinyl polymer and the isolation of the spongy divinyl polymer was carried out in an atmosphere of nitrogen [1].

Found %: C 88.15, 88.15; H 11.19, 11.12. $(C_4H_6)_x$. Calculated %: C 88.89, H 11.11.

Twelve g of spongy divinyl polymer, containing 10.58 g of carbon, was ozonized in ethyl acetate at -30°. The ozonide obtained was soluble in ethyl acetate. The solvent was distilled off from the polymer at 18 mm and 20°. The ozonide was dissolved in glacial acetic acid and decomposed with acetyl hydroperoxide. The excess acetyl hydroperoxide was destroyed with platinum black. The acetic acid was distilled off from the products of oxidative decomposition of the ozonide at 4 mm until the acids reached constant weight. We obtained 18.86 g of liquid and crystalline acids. The crystalline acids were separated from the liquid with diethyl ether. After removal of the diethyl ether, we obtained 8.51 g of liquid acids containing 3.72 g of carbon, and 10.35 g of crystalline acids containing 4.15 g of carbon. The acids obtained contained 7.87 g of carbon or 74.4% of the carbon skeleton of the polymer.

Found %: C 43.46, 43.88; H 5.09, 5.43.

The loss of polymer carbon skeleton during the oxidative decomposition of the ozonide with acetyl hydroperoxide was 2.71 g or 25.6%.*

After recrystallization from hot water, the crystalline acids melted at 183°, and a mixture with succinic acid (m. p. 183°) melted at 183°. The neutralization equivalent of the succinic acid isolated was determined as 59.

As the support for partition chromatography for separation of the acids, we used silica gel of MSK (fine silica gel of coarse porosity) grade of the Voskresenskii Chemical Combine [8]. As the stationary solvent we used water and for the mobile one, a mixture of chloroform and butyl alcohol, first saturated with water. In a column 480 mm long and 19 mm in diameter, we placed 25 g of silica gel (100-170 mesh), previously ground with 25 ml of water. The height of the silica gel layer in the column was 183 mm. The column was washed with chloroform to attain equilibrium on the surface. The mixture of liquid acids (0.9886 g) was dissolved in 10 ml of isoamyl alcohol. For the separation, 1.6 ml of the solution was taken with a pipette and introduced into the column carefully so that the surface of the silica gel was not disrupted. The acids were eluted from the column at a rate of 1 ml per minute with solutions of butanol in chloroform and titrated in 3 ml portions with a 0.0020 N solution of alkali in methyl alcohol. Phenolphthalein was used as the indicator. The polarity of the developer was gradually increased. The system of developers used was $CHCl_3$, 2, 4, 7, 10, 15, 20, 25, 30, 35, 50 % butanol in chloroform. From the chromatograms plotted from the titration data, we were able to calculate the amount of each acid in the mixture (Tables 4 and 5).

TABLE 3

	Peak volume of acids				
	levulinic	formic	succinic	butane-1,2,4-tricarboxylic	propane 1,2,3-tricarboxylic
In standard mixture of acids	52	119	165	214	272
In liquid acids	52	114	165	218	272

The chromatogram of the liquid acids is shown in Fig. 1 (chromatogram 1). The amount of alkali in milliliters, consumed in the titration of 3 ml of acid is plotted along the ordinate and the amount of developer in milliliters leaving the column along the abscissa.

To characterize the liquid acids we plotted a chromatogram of a mixture of those acids which we had previously found in the ozonolysis products of spongy divinyl polymer and also propane-1,2,3-tricarboxylic and levulinic acids, whose presence in the ozonolysis products might have been expected (Fig. 1, chromatogram 2). Later on this mixture of acids is refered to as the "standard" mixture of acids.

The composition of the standard mixture of acids (in g) was: formic 0.0023, levulinic 0.0106, succinic 0.0162, butane-1,2,4-tricarboxylic 0.0170 and propane-1,2,3-tricarboxylic 0.0085.

The separation of the "standard" mixture of the acids was performed with the same developer system as in the separation of the liquid acids obtained from the oxidative decomposition of the ozonide. The acids were identified by the peak volume [9].

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*Part of the loss was due to HCOOH and the volatile products of anomalous ozonolysis. The spongy divinyl polymer contained 22.8% of the units 1,2 and therefore 5.7% of the carbon skeleton of the polyer was lost as HCOOH during the ozonolysis.

TABLE 4

Peak No. (Fig. 2)	Name of acid	Amount (mg)		Acids in crystalline acids (g)
		NaOH	acid in sample	
III	Levulinic	0.09	0.26	0.143
IV	Acetic	0.36	0.39	0.215
V	Succinic	12.15	17.23	9.380
VI	Butane-1,2,4-tricarboxylic	0.42	0.65	0.358
VII	Hexane-1,x,y,6-tetracarboxylic	0.25	0.24	0.135

Footnote: The weight of crystalline acids taken for the separation was 0.0190 g.

The peak volumes of levulinic, succinic and propane-1,2,3,4-tricarboxylic acids agreed with the peak volumes of the same acids in the standard mixture. The peak volumes of formic and butane-1,2,4-tricarboxylic acids disagreed slightly. This could have been the result of insufficient uniformity during development of the chromatograms; for example, differences in the flow rate of the mobile solvent. The order in which the acids emerged from the column was always preserved.

TABLE 5

Peak No. (Fig. 1)	Name of acid	Chromatogram 1			Chromatogram 1a			Amount of acids in liquid acids isolated (g)
		amount (mg)			amount (mg)			
		NaOH	acids in sample	acids in 1 g of liquid acids	NaOH	acids in sample	acids in 1 g of liquid acids	
I	—	3.04	—	—	9.10	—	—	—
II	Propionic	2.27	4.2	25.1	1.97	3.64	23.4	0.206
III	Levulinic	4.30	12.5	76.9	4.65	13. 5	86.6	0.699
IV	Acetic	5.18	7.75	53.1	3.45	5.10	47.6	0.427
V	—	1.64	—	—	1.71	—	—	—
VI	Formic	4.48	5.15	31.6	3.90	4.48	28.8	0.256
VII	Succinic	12.17	17.82	114.9	12.17	17.82	114.9	0.956
VIII	Butane-1,2,4-tricarboxylic	36.20	57.20	351.8	34.2	54.20	348.5	2.975
IX	Propane-1,2,3-tricarboxylic	6.12	8.96	56.5	5.98	8.78	55.10	0.475
X	Hexane-1,x,y,6-tetracarboxylic	1.15	1.87	11.5	0.90	1.51	9.80	0.091

Footnote: Weight of liquid acids taken for the separation, 0.1626, 0.1553 g.
Chromatogram 1 was similar to chromatogram 1a.

The oxidative decomposition of the ozonide of the spongy divinyl polymer was carried out in glacial acetic acid and therefore, the presence of the latter in the liquid acids was unavoidable. In order to prove which of the peaks on chromatogram 1 corresponded to acetic acid, acetic and levulinic acids were added to a solution of the liquid acids and chromatogram 3 (Fig. 1) plotted and from this it was obvious that acetic acid corresponded to peak IV and levulinic to peak III.

Thus, on the chromatogram of the liquid acids, isolated from the products of oxidative decomposition of the ozonide of spongy divinyl polymer, peak II corresponded to propionic acid,* peak III – levulinic acid, peak IV – acetic acid, peak VI – formic, peak VII – succinic, peak VIII – butane-1,2,4-tricarboxylic, peak IX – propane-1,2,3-tricarboxylic, peak X – hexane-1,x,y,6-tetracarboxylic acids.* The first peak may contain acid esters of the acids as the latter were dissolved in tertiary amyl alcohol. In addition, Stoll [10] showed that in the ozonization of ethylene compounds in ethyl acetate, esters of the acids were found. If we assume that an analogous process occurs in the ozonolysis of caoutchoucs in ethyl acetate also, then the esters thus formed (neutral and acid) would contain carbon from the polymer skeleton, for which we had not allowed. The nature of the acid in peak VI was not established, but hypothetically it could have been glutaric acid, which could have been formed by the anomalous ozonolysis of a portion -1,4-1,2-1,4-, similar to the formation of glutaric acid observed by Zigler [11] in the ozonolysis of cyclohexene.

The separation of the crystalline acids, isolated from the ozonolysis of spongy divinyl polymer, was carried out with same system of developers.

Among the crystalline acids, succinic acid predominated and emerged on washing the column with a 20% mixture of butanol in chloroform (91.1% of the acids taken for analysis); the other acids were present in very small amounts. There were no other acids in the acetic acid distilled from the decomposition products of the ozonide. The results of the calculation of the amount of acids, found in the products of oxidative decomposition of the ozonide of spongy divinyl polymer, from the chromatograms for the separation of the liquid and crystalline acids are given in Tables 4 and 5.

SUMMARY

1. Using partition chromatography, we established that the oxidative decomposition products of the ozonide of spongy divinyl polymer contained, in addition to the acids isolated previously [1], levulinic and propane-1,2,3-tricarboxylic acids.

2. Propane-1,2,3-tricarboxylic acid was formed from the sections of the spongy polymer macromolecules, branched at the α-methylene groups, and this confirms the mechanism for the formation of the spongy polymer, proposed by Kahrach [3].

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Received December 21, 1956

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*From the separation of the acids, obtained from the ozonolysis products of divinyl caoutchouc, it was established that the acid emerging on washing the column with 2% butanol was propionic and the acid emerging on washing the column with 50% butanol was hexane-1,x,y,6-tetracarboxylic acid.

**Original Russian pagination. See C. B. Translation.

CONDENSATION OF ω-BROMOACETOPHENONE WITH DIETHANOLAMINE

B. M. Mikhailov and A. N. Makarova

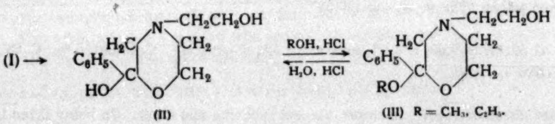
By mixing ω-chloroacetophenone with diethanolamine, Brighton and Reid [1] obtained a substance, with m. p. 44°, to which they assigned a chain structure and considered it as di-β-hydroxyethylaminoacetophenone (I). The authors did not investigate the chemical properties of the condensation product.

$$C_6H_5CO{-}CH_2Cl + NH(CH_2CH_2OH)_2 \rightarrow \underset{(I)}{C_6H_5COCH_2N(CH_2{-}CH_2OH)_2}$$

Later a series of authors [2-4] found that oxocyclotautomerism was inherent in such hydroxyamino ketones and that the equilibrium was displaced mainly towards the cyclic form. The condensation product of chloroacetone and diethanolamine also had a cyclic form, as we showed in a previous report [5].

In connection with this, it seemed interesting to study the properties of the condensation product of a ω-haloacetophenone with diethanolamine and to determine whether it actually has a chain structure, as put forward by Brighton and Reid, or whether it is a cyclic compound.

We prepared this substance by adding an ether solution of ω-bromoacetophenone to diethanolamine. The reaction proceeded quite smoothly and gave a good yield of a substance with m. p. 77-78°, and not 44°, as reported by Brighton and Reid. Investigation of the chemical properties of the substance obtained indicated that it was not a hydroxyamino ketone (I), but its tautomeric form, a cyclic semiacetal, 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II).



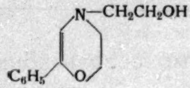
(II)

(III) R = CH₃, C₂H₅.

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II) was less stable than the corresponding 2-methyl compound [5]. When stored at room temperature it turned yellow and resinified. When recrystallized from water, the substance formed a molecular compound with water. The hydrate was unstable as it readily lost water when heated or in a vacuum desiccator. The semiacetal (II) hydrochloride, prepared by passing hydrogen chloride into an ether solution, reacted with anhydrous ethyl alcohol to give the hydrochloride of the acetal 2-phenyl-2-ethoxy-4-β-hydroxethylmorpholine (III, R = C_2H_5). The base was readily isolated from the salt by neutralizing it with an aqueous solution of potassium carbonate. The acetal hydrochloride (III, R = C_2H_5) was hydrolyzed to form the semiacetal (II) when heated in water for a short time at 70°. The semiacetal (II) hydrochloride was even more readily esterified with methyl alcohol. The acetal (III, R = CH_3) was isolated from its hydrochloride with potassium carbonate and characterized in the form of the methiodide and picrate.

The semiacetal (II) did not form a semicarbazone. When treated with semicarbazide it formed a solid substance with a high nitrogen content. The same nitrogenous substance was obtained by treating the acetal

(III, R = C_2H_5) with semicarbazide. However, the semiacetal (II) reacted with some reagents as a typical α-amino ketone. Thus, it rapidly reduced Fehling's solution and an ammonia solution of silver oxide at room temperature. Under these conditions, acetal (III) did not reduce Fehling's solution. When heated with concentrated hydrochloric acid in the semiacetal (II) eliminated water and was converted to 2-phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine-1,4 (IV).



(IV)

EXPERIMENTAL

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II). Over a period of 1.5 hours, a solution of 10 g (0.05 mole) of ω-bromoacetophenone in 50 ml of absolute ether was added dropwise with stirring to 11.2 g (0.1 mole) of diethanolamine. During this time the temperature did not exceed 20-24°. The reaction mixture which consisted of two layers (the upper, slightly yellowish and the lower, thick and yellow), was left at room temperature overnight. Then, after boiling for 30 minutes, the ether layer a poured off from the thick mass and the latter extracted with ether. The ether was distilled off from the combined ether solutions. The residual oil crystallized on standing in the cold. The yield of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was 10.3 g (90.%). The m. p. was 72-74°. After two recrystallizations from benzene, the substance had m. p. 77-78°.

Found %: C 64.59; H 7.61; N 6.20; active H 0.85. $C_{12}H_{17}O_3N$. Calculated %: C 64.55; H 7.64; N 6.27 active 2H 0.90.

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine (II) was soluble in water, alcohols, benzene, acetone and chloroform; it was difficultly soluble in ether. The substance turned yellow and formed tar during storage at room temperature, but was stable to storage in the cold. It readily reduced an ammonia solution of silver oxide at room temperature (with the formation of a silver mirror) and Fehling's solution. Passing dry hydrogen chloride through an ether solution of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine gave a flocculent precipitate of the hygroscopic hydrochloride.

2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrate. This was prepared by recrystallizing the substance (II) from water. The m. p. was 50-51°.

Found %: C 59.77; H 8.05; N 6.07; active H 1.21. $C_{12}H_{19}O_4N$. Calculated %: C 59.73; H 7.93; N 5.81; active 3H 1.25.

The hydrate dissolved readily in water, alcohol, acetone and ether. On being dried in vacuum for 0.5 hours, it lost water and was converted into substance (II).

The action of semicarbazide on 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine. A mixture of 1 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine, 1.5 g of semicarbazide hydrochloride, 1.5 g of sodium acetate and 5 ml of water was boiled for 1 hour. The precipitate from the solution was recrystallized twice from dilute alcohol. The material obtained was a yellowish powder with m. p. 231-232° (decomp.). The material was very difficultly soluble in water and alcohols.

Found %: C 32.36; H 5.20; N 39.56.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride. A mixture of the hydrochloride, prepared from 5 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine, 20 ml of anhydrous ethyl alcohol and 1.2 ml of ethyl alcohol, saturated with hydrogen chloride, was boiled for 30 minutes. After distilling off 15 ml of alcohol, we added ether to the cooled residue until the solution became turbid. Crystals with m. p. 122-124° were isolated. The yield was 95%. After two recrystallizations from a mixture of alcohol and ether, the substance had m. p. 125-126°. The hydrochloride of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine was readily soluble in water and alcohols.

Found %: C 58.21; H 7.67. $C_{14}H_{22}O_3NCl$. Calculated %: C 58.41; H 7.70.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine (III, R = C_2H_5). An aqueous solution of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride was neutralized with potassium carbonate. The liberated base was extracted with ether and the extract dried over potassium carbonate. The ether was distilled off to leave an oil, which crystallized on cooling. The m. p. was 55-57°. The yield was 85%. After recrystallization from ethyl ether, benzene or a mixture of benzene and petroleum ether, the substance had m. p. 61.5-62.5°.

Found %: C 66.89; H 8.50; N 5.73; active H 0.45. $C_{14}H_{21}O_3N$. Calculated %: C 66.74; H 8.42; N 5.57; active H 0.40.

2-Phenyl-2-ethoxy-4-β-hydroxyethylmorpholine was very readily soluble in water and the usual organic solvents and did not reduce an ammonia solution of silver oxide at room temperature or Fehling's solution. On boiling 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine with semicarbazide, we obtained the same substance as from the treatment of substance (II) with semicarbazide.

Hydrolysis of 2-phenyl-2-ethoxy-4-β-hydroxyethylmorpholine hydrochloride. An aqueous solution of 3.4 g of the hydrochloride was heated for 30 minutes at 70°. After cooling, the solution was neutralized with potassium carbonate and extracted with ether. The ether solution was dried over potassium carbonate. The ether was distilled off and the residual oil crystallized. The m. p. was 42-45°. The yield was 1.7 g (63%). After recrystallization from water, the substance had m. p. 50-51°. A mixed melting point of the substance obtained with 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrate was not depressed.

2-Phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride. On adding anhydrous methyl alcohol to 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine hydrochloride, we obtained a quantitative yield of 2-phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride. After two recrystallizations from a mixture of methyl alcohol and ether, the substance formed lustrous plates with m. p. 142-143°. The hydrochloride was very readily soluble in water and alcohols.

Found %: C 57.14; H 7.38; N 13.06. $C_{13}H_{20}O_3NCl$. Calculated %: C 57.01; H 7.36; N 12.95.

2-Phenyl-2-methoxy-4-β-hydroxyethylmorpholine (III, R = CH_3). An aqueous solution of 2-phenyl-2-methoxy-4-β-hydroxyethylmorpholine hydrochloride was saturated with potassium carbonate. The base was extracted with ether. The ether solution was dried with potassium carbonate and then the solvent distilled off. An oily substance was obtained. The yield was 85%.

The methiodide had m. p. 159-160°, after recrystallization from alcohol.

Found %: C 44.15; H 5.93. $C_{14}H_{22}O_3NI$. Calculated %: C 44.33; H 5.85.

The picrate had m. p. 112-113°, after recrystallization from alcohol.

Found %: C 48.76; H 4.91; N 12.18. $C_{19}H_{22}O_{10}N_4$. Calculated %: C 48.93; H 4.76; N 12.02.

2-Phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine (IV). 1.5 g of 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was heated at 120° for 15 minutes. Then three drops of concentrated hydrochloric acid was added. The temperature rose to 160° at this. The thick, red-brown mass was distilled. We obtained 0.5 g of a substance with b. p. 185-188° (3 mm). The substance reacted with methyl iodide to give a methiodide, which was recrystallized from ethyl alcohol. The m. p. was 121-122°. The methiodide was readily soluble in alcohols and insoluble in ether.

Found %: C 44.78; H 5.22; N 3.96. $C_{13}H_{18}O_2NI$. Calculated %: C 44.96; H 5.22; N 4.03.

SUMMARY

1. ω-Bromoacetophenone reacted with diethanolamine to give a cyclic semiacetal, 2-phenyl-2-hydroxy-4-β-hydroxyethylmorpholine.

2. 2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine esterified smoothly with alcohol. The alkoxyl derivative formed was readily hydrolyzed to the initial hydroxy compound.

3. 2-Phenyl-2-hydroxy-4-β-hydroxyethylmorpholine was dehydrated by heating to give 2-phenyl-4-β-hydroxyethyl-5,6-dihydrooxazine-1,4.

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Institute of Experimental Cancer Pathology
and Therapy

Received January 2, 1957

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*Original Russian pagination. See C. B. Translation.

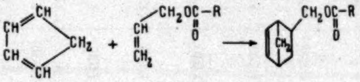
ORGANIC INSECTOFUNGICIDES

XXVIII. THE SYNTHESIS OF SOME ESTERS OF BICYCLO-(2,2,1)-HEPTENYL-5-CARBINOL-2•

S. S. Kukalenko and N. N. Mel'nikov

In recent years various polycyclic compounds, prepared by diene synthesis from cyclopentadiene and hexachlorocyclopentadiene have attracted the attention of investigators, as very active insecticides were found among them [1-6]. We undertook the synthesis of this type of compound in order to study the relation of the insecticide activity of the polycyclic compounds to their structure. First at all, we undertook the synthesis of various esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 by reacting cyclopentadiene with allyl esters of various acids. The preparation of such derivatives is of doubtless interest as up to now the condensation of cyclopentadiene only with allyl alcohol, allyl chloride and bromide [7], some vinyl ethers [8], acrolein [9], acetylene [10, 11] and a small number of various other compounds [12, 13] has been described in the literature.

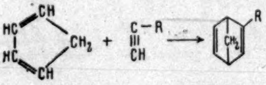
Cyclopentadiene reacted with the allyl esters of various acids at a high temperature in an autoclave or sealed tubes under some pressure, as with the reactions of cyclopentadiene with the majority of other unsaturated compounds. The reaction may be represented by the following general scheme:



$R = CH_3, C_2H_5, C_3H_7, C_3H_7$-изо$, C_6H_5, CH_2Cl, CH_2SCN$.

The compounds we prepared and their properties are listed in the table. As only the boiling points are given in the literature for the condensation products of cyclopentadiene with allyl alcohol and allyl bromide and chloride, we synthesized these products as well and also 2,3-dichlorobicyclo-(2,2,1)-heptene-5 from transdichloroethylene and cyclopentadiene.

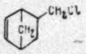
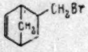
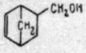
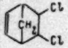
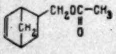
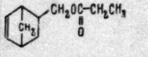
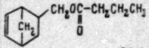
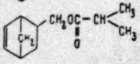
In order to prepare various arylbicyclo-(2,2,1)-heptadienes, we studied the reaction of cyclopentadiene with phenyl-, chlorophenyl-, bromophenyl- and tolylacetylenes. In this case we could expect reactions by the following scheme



$R = C_6H_5, C_3H_4Cl, C_6H_4Br, C_6H_4CH_3$.

However, up to now we have not been able to isolate monomeric reaction products and isolated only solid polymeric substances with high molecular weights, whose structure has not yet been established.

• From S. S. Kukalenko's Candidate Thesis.

Substance No.	Formula	Yield (%)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Analysis data (%)					
						found	calculated	found			calculated		
								C	H	Cl	C	H	Cl
(I)*		49	51—52.5° (9)	1.070	1.4940	38.77	39.14	—	—	—	—	—	—
(II)*		58	77—79 (15)	1.370	1.5210	41.68	42.04	—	—	—	—	—	—
(III)*		42	67—70 (2.5)	1.040	1.5028	35.24	34.70	—	—	—	—	—	—
(IV)*		26.5	67—70 (8)	1.230	1.5110	39.70	39.39	—	—	—	—	—	—
(V)		60	83.5—84 (7)	1.035	1.4754	45.17	45.05	71.87, 71.79	8.99, 8.75	—	72.28	8.43	—
(VI)		59	98—100 (11)	1.033	1.4760	49.14	49.67	73.48, 73.26	8.99, 8.95	—	73.33	8.88	—
(VII)		56	114—115 (11—11.5)	1.016	1.4765	53.89	54.28	73.72, 73.74	9.27; 9.13	—	74.22	9.27	—
(VIII)		50	99 (6)	0.990	1.4670	54.39	54.28	73.62, 73.48	9.54, 9.30	—	74.22	9.27	—

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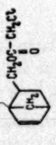
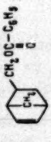
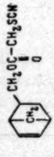
* According to the literature data [7] for substances: (I) b. p. 54-57° (11 mm), (II) 75-77° (13 mm), (III) 92-95° (13 mm); according to [13] for substance (IV) b. p. 83-85° (22 mm).

(continuation)

Substance No.	Formula	Yield (%)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Analysis data (%) found C	found H	found Cl	calculated C	calculated H	calculated Cl
(IX)		48	127–128 (10)	1.172	1.4980	50.14	49.92	—	—	17.85, 18.20	—	—	17.70
(X)		61	186–187 (17)	1.103	1.5410	64.94	64.53	78.40, 78.39	7.23, 7.19	—	78.94	7.02	—
(XI)		70	154–156 (2)	1.184	1.5212	57.41	57.55	58.96, 58.84	5.99, 5.74	—	59.19	5.83	—

EXPERIMENTAL

The condensation of cyclopentadiene with the various unsaturated compounds proceeded at 160-195° over a period of 7-12 hours. An equimolecular mixture of cyclopentadiene and the other unsaturated compound was sealed in a glass tube and heated in a steel autoclave for 7-12 hours at the given temperature. At the end of the reaction, the reaction mixture was carefully fractionated in vacuum. The compounds obtained and their properties are given in the table.

The reaction of arylacetylenes with cyclopentadiene proceeded under the same conditions. After distilling off the unreacted starting materials and dicyclopentadiene in vacuum, we purified the solid substances obtained by reprecipitation from a suitable solvent and analyzed them.

SUMMARY

The reaction of cyclopentadiene with various esters of allyl alcohol was studied. A series of derivatives of bicyclo-(2,2,1)-heptenyl-5-carbinol-2, that are not described in the literature, were synthesized.

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Scientific Institute on Fertilizers and
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Received December 18, 1956

ORGANIC INSECTOFUNGICIDES

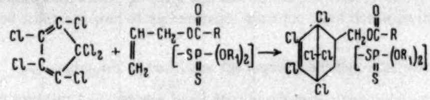
XXIX. THE REACTION OF HEXACHLOROCYCLOPENTADIENE WITH SOME UNSATURATED COMPOUNDS*

S. S. Kukalenko and N. N. Mel'nikov

Although hexachlorocyclopentadiene has a somewhat lower reactivity than cyclopentadiene, as is known, it is still capable of reacting with various unsaturated compounds either of the aliphatic or alicyclic series. Thus, it reacts relatively readily with vinyl chloride, cyclopentadiene, cyclopentene, bicycloheptene, bicycloheptadiene and certain other compounds [1-4]. Many of the compounds prepared by diene synthesis from hexachlorocyclopentadiene have been used practically in agriculture against plant pests and in industry for the manufacture of plastics [5-7]. Of these compounds the major ones are as follows: chlorodan, heptachlorine, aldrin, dieldrin, isodrin and endrin, which are used as insecticides against the most varied harmful insects. Doubtlessly, further study of the hexachlorocyclopentadiene reaction will make it possible to synthesize valuable new compounds which will find use in a wide range of agricultural fields.

In order to find new active insecticides, we studied the reaction products of hexachlorocyclopentadiene with various unsaturated compounds and, first of all, with some esters of allyl alcohol and bicyclo-(2,2,1)-heptenyl-5-carbinol-2. In addition, we studied the reactions of hexachlorocyclopentadiene with ethyl and isobutyl vinyl ethers which M. F. Shostakovskii kindly gave us, and we would like to take this opportunity to thank him.

The allyl esters of various carboxylic acids and dialkylallyl esters of dithiophosphoric acid reacted quite readily with hexachlorocyclopentadiene on heating equimolecular amounts of the starting materials at 100-125° for 10-12 hours and the corresponding adducts were obtained in 50-60% yields. These reactions may be represented by the following general scheme (I).



$R = CH_3, C_2H_5, C_3H_7, C_3H_7$ - iso, CH_2Cl, C_6H_5.

$R_1 = C_2H_5$.

The compounds we obtained and their properties are listed in the table. It should be noted that some of the compounds given in the table are described in the literature, but they were either prepared by different methods or no constants were given for them.

Hexachlorocyclopentadiene condensed much more slowly with esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 and the reaction mixture had to be heated for not less than 15 hours at 125-130° to obtain a 50% adduct yield. Hexachlorocyclopentadiene reacted with esters of bicyclo-(2,2,1)-heptenyl-5-carbinol-2 by scheme (II).

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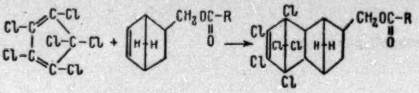
* From S. S. Kukalenko's Candidate Thesis.



$R = CH_3, CH_2CH_3, C_3H_7, C_3H_7\text{-iso}, CH_2Cl, C_6H_5.$

The compounds we obtained and their properties are listed in the table.

Of the compounds studied, the vinyl ethers reacted most readily with hexachlorocyclopentadiene as they were added at 80-90° while the bicyclic compounds reacted with hexachlorocyclopentadiene much more slowly and at a higher temperature.

A study of the insecticide properties of the compounds we synthesized showed that they were much less active than aldrin and even chlorindan (1,2,4,5,6,7,8,8-octachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan).

EXPERIMENTAL

Condensation of hexachlorocyclopentadiene with allyl esters. For the preparation of the esters of 1,2,3,4,7,7-hexachlorobicyclo-(2,2,1)-heptenyl-2-carbinol-6 equilimolecular mixtures of hexachlorocyclopentadiene and the appropriate allyl ester were heated in sealed tubes at 105-110° for 10-12 hours (excluding only the condensation of hexachlorocyclopentadiene with diethylallyl dithiophosphate, when the condensation was performed at 120-125°). After heating and cooling, the tubes were opened and the reaction products carefully fractionated in vacuum not less than twice and analyzed. We should note that the acetate and propionate of 1,2,3,4,7,7-hexachlorobicyclo-(2,2,1)-heptenyl-2-carbinol-6 were recently described by McBee et al. [8], but they were prepared by other methods. The corresponding butyrate is also described in the literature [9]. The compounds we synthesized and their properties are listed in the table.

Condensation of hexachlorocyclopentadiene with esters of bicyclo-(2,2,1)-heptenyl-2-carbinol-5. An equimolecular mixture of hexachlorocyclopentadiene and bicyclo-(2,2,1)-heptenyl-2-carbinol-5 was heated at 125-130° for 15 hours. After the reaction, the reaction mixture was either fractionated in high vacuum or treated with a small amount of methyl alcohol after cooling. In the latter case, the crystalline product which separated was filtered off and recrystallized from an appropriate solvent. In the case of the benzoate we synthesized, which was a viscous liquid, distillation in high vacuum was accompanied by some decomposition and it was therefore purified by passing a benzene solution through a chromatography column filled with active aluminum oxide. After distilling off the benzene in vacuum, we obtained an analytically pure sample. We should note, however, that this compound and also the others we synthesized, could exist in the form of several stereoisomers, which have not been separated up to now and must be the subject of further investigation.

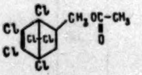
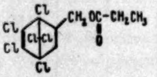
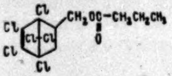
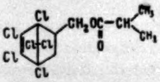
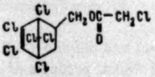
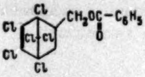
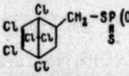
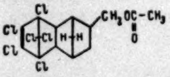
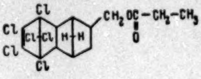
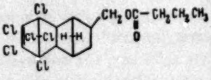
The substances we prepared and their properties are listed in the table.

Condensation of hexachlorocyclopentadiene with vinyl ethers. a) A mixture of 16.4 g of hexachlorocyclopentadiene and 5 g of ethyl vinyl ether was heated in a sealed tube at 80-90° for 6 hours. At the end of the reaction and after cooling, the product obtained was fractionated. As a result of the fractionation we isolated 2 g of unreacted ethyl vinyl ether, 8 g of hexachlorocyclopentadiene and 7.5 g of adduct [1,2,3,4,7,7-hexachloro-5-ethoxybicyclo-(2,2,1)-heptene-2].

B. p. 134-135° (5 mm) d_4^{20} 1.5576, n_D^{20} 1.5358, MR_D 68.98; calc. 69.34.

Found %: C 31.56, 31.48; H 2.43, 2.61; Cl 61.96, 61.47. $C_9H_8OCl_6$. Calculated %: C 31.30; H 2.31; Cl 61.73.

b) A mixture of 5 g of vinyl isobutyl ether and 13.6 g of hexachlorocyclopentadiene was heated in a sealed tube at 110° for 8 hours. At the end of the reaction, the mixture obtained was fractionated in vacuum. We isolated 3 g of vinyl isobutyl ether, 8 g of hexachlorocyclopentadiene and 5 g of 1,2,3,4,7,7-hexachloro-5-isobutoxybicyclo-(2,2,1)-heptene-2.

Formula	Boiling point (mm pressure)	Yield (%)	d_4^{20}	n_D^{20}	MR_D		Cl (%)	
					found	calc.	found	calc.
	178—179° (8.5—9) *	47	1.5630	1.5340	74.13	74.25	57.43, 57.00	57.10
	162—163 (1.5) **	54	1.5280	1.5328	7856	78.77	55.2, 55.12	55.03
	156—157 (0.4) ***	60	1.4850	1.5280	83.58	83.77	53.81, 53.85	53.11
	186—187 (6.5)	49	1.4950	1.5310	8341	83.77	53.56, 53.83	53.11
	173—174 (0.4)	39	1.6500	1.5510	78.79	79.12	61.01, 61.35	60.90
	196—197 (0.4) m.p. 65—66°	31	—	—	—	—	48.77, 49.35	48.96
	—	56	1.4859	1.5660	109.6	110.3	40.31, 40.88	40.41
	185—187 (0.7) m.p. 78—79°	50	—	—	—	—	49.10, 49.07	48.50
	182—183 (0.2)	42	1.4791	1.5498	97.54	97.56	46.82, 47.03	47.02
	198—199 (0.75) m.p. 74—75°	43	—	—	—	—	46.11, 45.89	45.61

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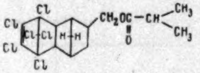
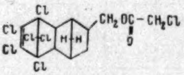
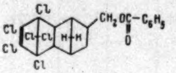
* According to the literature data [8]: b. p. 154-155° (2 mm), n_D^{20} 1.533.

** According to the literature data [8]: b. p. 160-161° (2 mm) n_D^{20} 1.532.

*** According to the literature data [8]: b. p. 158-159° (0.5 mm) n_D^{20} 1.527.

(continuation)

Formula	Boiling point (mm pressure)	Yield (%)	d_4^{20}	n_D^{20}	MR_D		Cl (%)	
					found	calc.	found	calc.
	186—187° (0.9) m.p. 86—87°	48	—	—	—	—	45.71, 46.07	45.61
	201—202 (0.2) m.p. 70—71°	34	—	—	—	—	52.23, 52.60	52.48
	227—228 (0.4)	48	1.4547	—	—	—	42.51, 42.16	42.59

B. p. 145-146° (4 mm), d_4^{20} 1.4460, n_D^{20} 1.5276, MR_D 79.30; calc. 78.98.

Found %: Cl 57.40, 56.88. $C_{11}H_{12}OCl_6$. Calculated %: Cl 57.11.

SUMMARY

The condensation of hexachlorocyclopentadiene with esters of allyl alcohol and bicyclo-(2,2,1)-heptenyl-2-carbinol-5 and vinyl ethers was studied. It was shown that this reaction gave normal products of diene synthesis, in which hexachlorocyclopentadiene reacted as a diene and the other unsaturated compounds as dienophils. A series of compounds, that have not been described in the literature were synthesized.

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[5] N. N. Mel'nikov and L. G. Vol'fson, Chem. Ind. 1953, 413.

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Scientific Institute on Fertilizers
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Received December 18, 1956

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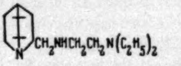
* Original Russian pagination. See C. B. Translation.

TERTIARY AMINES OF SOME HETEROCYCLICS AS POSSIBLE HYPOTENSION REMEDIES

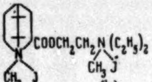
E. S. Nikitskaia, V. S. Usovskaia and M. V. Rubtsov

Until recently, in searching for ganglioblocking media, special attention was paid to quaternary ammonia salts as among them are compounds which are used practically in medicine [1]. It was considered that the ganglioblocking effect was due to the quaternary nitrogen. However, factual material that has collected shows that compounds with a similar effect are also found among certain tertiary and secondary amines. In 1950 M. D. Mashkovsky et al., made the first observations of this nature [2]. Later, analogous data appeared in the foreign literature [3].

A recent study of quinuclidine derivatives [4], that we synthesized, showed the very high ganglioblocking activity of a series of compounds that were secondary-tertiary amines. Thus, for example, 2-diethylamino-ethylaminomethylquinuclidine (a) has a high ganglioblocking effect similiar to that of the dimethiodide of the diethylaminoethyl ester of α-quinuclidinecarboxylic acid (b), described previously [1].

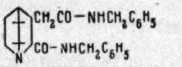


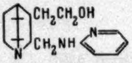
(a)



(b)

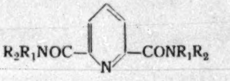
Other substituted quinuclidines, which are secondary-tertiary amines, such as the dibenzylamide of [2-carboxyquinuclidyl-(3)]-acetic acid [5] and 2-[(pyridyl-2')-aminomethyl]-3-(β-hydroxyethyl)-quinuclidine [6] were also found to be highly active.





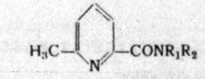
As compounds with a ganglioblocking effect have a definite value in hypertonia therapy, it seemed advantageous to continue the investigations in order to find simpler compounds. The preparation of analogous amines of the pyridine and piperidine series was especially interesting as our previous investigation showed that the substitution of a piperidine for a quinuclidine ring hardly affected the character and activity of this type of preparation. For this reason we synthesized a series of compounds of the pyridine and piperidine series.

The starting substances were dipicolinic and 6-methylpicolinic acids, prepared by oxidizing 2,6-lutidine, which is a waste product in phthivazide production. The chlorides or esters of these acids reacted with various amines to give the corresponding amides (I and II).



(I)

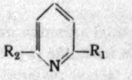
(a) $R_1 = R_2 = CH_3$; (b) $R_1 = R_2 = C_2H_5$;
(c) $R_1 = H$; $R_2 = CH_2CH_2N(C_2H_5)_2$;
(d) $R_1 = H$; $R_2 = CH(CH_3)(CH_2)_3N(C_2H_5)_2$;
(e) $R_1 = H$; $R_2 = CH_2C_6H_5$;
(f) $R_1 = H$; $R_2 = \alpha$-pyridyl



(II)

(a) $R = H$; $R_2 = CH_2CH_2N(C_2H_5)_2$;
(b) $R = H$; $R_2 = CH_2C_6H_5$;
(c) $R = H$; $R_2 =$ A-pyridyl

Contrary to literature reports that amines cannot be prepared from pyridinecarboxylic amides using lithium aluminum hydride, we were able to convert most of the amides obtained into amines (III).

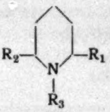


(III)

(a) $R_1 = R_2 = CH_2N(C_2H_5)_2$;
(b) $R_1 = R_2 = CH_2NHCH_2C_6H_5$;
(c) $P_1 = R_2 = CH_2NH(\alpha\text{-}C_5H_4N)$;
(d) $R_1 = CH_3$; $R_2 = CH_2NHCH_2C_6H_5$;
(e) $R_1 = CH_3$; $R_2 = CH_2NH(\alpha\text{-}C_5H_4N)$.

However, the reaction proceeded with the formation of side products and gave, as a rule, low amine yields.

The piperidinecarboxylic amides could be reduced much better. In this case good yields of amines were obtained and they could be isolated without difficulty. This made it possible to prepare the corresponding amino derivatives of the piperidine series (IV).



(IV)

(a) $R_1 = R_2 = CH_2N(C_2H_5)_2$; $R_3 = H$;
(b) $R_1 = R_2 = CH_2N(C_2H_5)_2$; $R_3 = CH_3$;
(c) $R_1 = CH_2NHCH_2C_6H_5$; $R_2 = CH_3$; $R_3 = H$;
(d) $R_1 = CH_2-\underset{\displaystyle CH_3}{\underset{|}{N}}-CH_2C_6H_5$; $R_2 = R_3 = CH_3$;
(e) $R_1 = CH_2NHCH_2CH_2N(C_2H_5)_2$; $R_2 = R_3 = CH_3$.

A pharmacological study, carried out by I. M. Sharapov in a pharmacological laboratory, on the pyridine and piperidine derivatives showed that 1,6-dimethyl-2-(β-diethylaminoethylaminomethyl)-piperidine (IV e) had a high ganglioblocking activity, 10 times greater than the tetraethylammonium iodide. The rest of the compounds had no value as ganglioblocking agents.

EXPERIMENTAL

Di-(dimethylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid [1], was gradually added to 120 ml of a 14.5% solution of dimethylamine in absolute ether. The reaction mixture was stirred for 8 hours at room temperature, then excess of a 50% solution of potassium carbonate was added and the solution extracted with ether. The ether extract was dried over baked potassium carbonate and the ether distilled off. We obtained 1.3 g (32%) of a white crystalline substance, which was soluble in the usual organic solvents and in water. The m. p. was 144-146°.

Found %: C 59.92; H 6.76; N 19.25. $C_{11}H_{15}O_2N_3$. Calculated %: C 59.71; H 6.83; N 18.99.

Di-(diethylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid was added to a solution of 26 g of diethylamine in 100 ml of absolute ether. The reaction mixture was treated as described above. We obtained 4.16 g (85%) of a substance with b. p. 170-172° (0.25 mm). The substance was soluble in the usual organic solvents and in water. On standing, the substance crystallized. The m. p. was 74.5-76.5° (from petroleum ether).

Found %: C 64.60; H 8.26; N 14.96. $C_{15}H_{23}O_2N_3$. Calculated %: C 64.95; H 8.35; N 15.22.

2,6-Di-(diethylaminomethyl)-pyridine. Three g of the di-(diethylamide) of dipicolinic acid was reduced for 20 hours with 1.23 g of lithium aluminum hydride in 100 ml of absolute ether under the conditions described previously [4]. We obtained 1.75 g (65%) of a straw-yellow, oily substance with b. p. 100-102° (0.35 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 72.41; H 10.79. $C_{15}H_{27}N_3$. Calculated %: C 72.23; H 10.91.

Di-(diethylamide) of dipipecolinic acid. 8.7 g of the di-(diethylamide) of dipicolinic acid was dissolved in 100 ml of anhydrous ethyl alcohol, 8 ml of a 15% alcohol solution of hydrogen chloride added and the solution hydrogenated at room temperature in the presence of 0.4 g of platinum oxide at a pressure of 40-60 cm of water. The hydrogenation was complete in 6 hours. The catalyst was filtered off and the filtrate evaporated to dryness in vacuum. The residue was treated with excess of a 50% potassium carbonate solution and extracted with ether. The ether extract was dried with baked potassium carbonate, the ether distilled off and the residue vacuum distilled. We obtained 7.5 g (84%) of an oily, colorless liquid with b. p. 175-177° (0.3 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 63.46; H 10.37; N 15.02. $C_{15}H_{29}O_2N_3$. Calculated %: C 63.56; H 10.31; N 14.82.

2,6-Di-(diethylaminomethyl)-piperidine. 3.5 g of di-(diethylamide) of dipipecolinic acid was reduced for 20 hours with 1.4 g of lithium aluminum hydride in 100 ml of absolute ether. We obtained 2.3 g (73%) of a yellowish liquid, which was soluble in the usual organic solvents and in water. The b. p. was 105° (0.5 mm).

Found %: C 70.70; H 12.74; N 16.17. $C_{15}H_{33}N_3$. Calculated %: C 70.52; H 13.02; N 16.45.

N-Methyl-2,6-di-(diethylaminomethyl)-piperidine. 2.2 g of 2,6-di-(diethylaminomethyl)-piperidine was heated on a boiling water bath for 15 hours with 0.83 g of 33.5% formalin, 1.49 g of formic acid and 1.32 ml of water. The reaction mixture was treated with excess of a 50% solution of potassium carbonate and extracted with ether. After drying the extract and distilling off the ether, we vacuum distilled the residue. We obtained 1.73 g (74%) of a colorless, mobile liquid with b. p. 84-86° (0.2 mm).

Found %: N 15.63, 15.72. $C_{16}H_{35}N_3$. Calculated %: N 15.59.

Di-(diethylaminoethylamide) of dipicolinic acid. From the diacid chloride, prepared from 6 g of dipicolinic acid, and using the method described for the synthesis of the di-(diethylamide) of dipicolinic acid, we prepared 9.38 g (72%) of a caramel-like, light yellow substance with b. p. 223-225° (0.6 mm), which was soluble in the usual organic solvents and in water.

Found %: C 62.38; H 8.96; N 19.31. $C_{19}H_{33}O_2N_5$. Calculated %: C 62.78; H 9.15; N 19.26.

Di-(diethylaminoisopentylamide) of dipicolinic acid. The diacid chloride, prepared from 3 g of dipicolinic acid, was treated as described above with 11.3 g of diethylaminoisopentylamine, dissolved in 100 ml of absolute ether. The yield was 5.6 g (70%). The b. p. was 225-227° (0.35 mm). The substance was soluble in the usual organic solvents and in water.

Found %: C 67.04; H 10.07. $C_{25}H_{45}O_2N_5$. Calculated %: C 67.07; H 10.37.

The dimethiodide was a white, hygroscopic substance with m. p. 125°.

Found %: N 9.22, 9.25; I 34.24. $C_{27}H_{51}O_2N_5I_2$. Calculated %: N 9.52; I 34.69.

The dibenzylamide of dipicolinic acid. 7.7 g of benzylamine, dissolved in 100 ml of absolute ether, was added to the diacid chloride dipicolinic acid prepared from 4 g of the acid. At the end of the reaction, the precipitate formed was filtered off, carefully washed with chloroform and the chloroform extract shaken twice with 25 ml of a 50% potassium carbonate solution, dried with baked potassium carbonate and the chloroform distilled off in vacuum. The solid residue was recrystallized from alcohol. We obtained 4.36 g (53%) of a substance, which was soluble in chloroform and hot water, difficultly soluble in ether and insoluble in water. The m. p. was 179-181.°

Found %: C 72.90; H 5.50; N 12.03, 12.08. $C_{21}H_{19}O_2N_3$. Calculated %: C 73.02; H 5.54; N 12.16.

2,6-Di-(benzylaminomethyl)-pyridine. 6.45 g of the dibenzylamide of dipicolinic acid was reduced for 20 hours with 2.13 g of lithium aluminum hydride in 120 ml of a mixture of absolute ether and benzene (1:1). We obtained 0.6 g (10%) of a light yellow, oily substance with b. p. 207° (0.5 mm), which was soluble in the usual organic solvents and insoluble in water. The bulk of the products (2-2.5 g) became tarry on distillation.

Found %: N 13.04, 13.26. $C_{21}H_{23}N_3$. Calculated %: N 13.23.

Di-(pyridyl-2)-amide of dipicolinic acid. 11.2 g of α-aminopyridine was added to the diacid chloride, prepared from 4 g of dipicolinic acid, dissolved in 50 ml of anhydrous benzene. The reaction mixture was heated for 3 hours at 60° and then cooled and the crystals formed filtered off, ground in a mortar with 25 ml of water, again filtered and washed with alcohol and ether. We obtained 4.3 g (56%) of colorless)crystals as small needles. The substance was insoluble in water, difficultly soluble in alcohol and ether and soluble in hot pyridine. The m. p. was 225-226°.

Found %: N 22.12, 21.87. $C_{17}H_{13}O_2N_5$. Calculated %: N 21.93.

2,6-Di-(pyridyl-2')-aminomethylpyridine. 3.1 g of the di-(dipyridyl-2')-amide of dipicolinic acid was reduced for 20 hours with 1.14 g of lithium aluminum hydride in 75 ml of a mixture of ether and toluene (1:2). We obtained 0.2 g (7%) of a substance with m. p. 147-149°, which was soluble in toluene, benzene and ethyl alcohol. 1.5 g of the starting diamide was isolated by extracting the precipitate of lithium and aluminum hydroxides with pyridine.

Found %: C 69.65; H 5.73; N 24.12, 24.28. $C_{17}H_{17}N_5$. Calculated %: C 70.07; H 5.88; N 24.05.

Diethylaminoethylamide of 6-methylpicolinic acid. The reaction was performed as in the case of the corresponding amide of dipicolinic acid. From the acid chloride, prepared from 4 g of 6-methylpicolinic acid, and 10 g of diethylaminoethylamine, dissolved in 100 ml of absolute ether, we obtained 4.4 g (64%) of a colorless, oily substance with b. p. 149-152° (0.5 mm), which was soluble in the usual organic solvents.

Found %: N 17.71, 18.08. $C_{13}H_{21}ON_3$. Calculated %: N 17.86.

Benzylamide of 6-methylpicolinic acid. The benzylamide of 6-methylpicolinic acid was synthesized by two methods.

a) The acid chloride, prepared from 3 g of 6-methylpicolinic acid, was treated with 7 g of benzylamine, dissolved in 100 ml of absolute ether. We obtained 2.15 g (43%) of a substance with b. p. 189-191° (0.4 mm). The white crystals were difficultly soluble in alcohol and ether and insoluble in water. The m. p. was 96-98°.

Found %: C 74.15, 74.32; H 6.23, 6.33; N 12.46. $C_{14}H_{14}ON_2$. Calculated %: C 74.30; H 6.23; N 12.38.

b) A mixture of 4 g of ethyl 6-methylpicolinate and 20 g of benzylamine was boiled for 48 hours. The yield was 2.94 g (54%). The m. p. was 96-98°. A mixture of the substance with the benzylamide, prepared via the acid chloride, did not show depression of melting point.

2-Methyl-6-benzylaminomethylpyridine. 2.95 g of the benzylamide of 6-methylpicolinic acid was reduced for 20 hours with 0.74 g of lithium aluminum hydride in 165 ml of absolute ether. We obtained 0.65 g of a substance (23%) with b. p. 119° (0.1 mm). The substance was soluble in organic solvents and insoluble in water.

Found %: N 13.05, 13.18. $C_{14}H_{16}N_2$. Calculated %: N 13.19.

Benzylamide of 6-methylpipecolinic acid. Five g of ethyl 6-methylpipecolinate [1] was boiled with 25 ml of freshly distilled benzylamine. The yield was 4.6 g (65%). The colorless, oily liquid, with low mobility, was readily soluble in the usual organic solvents and insoluble in water. The b. p. was 164-166° (0.35 mm).

Found %: C 72.34, 72.18; H 8.40, 8.50. $C_{14}H_{20}ON_2$. Calculated %: C 72.37; H 8.67.

2-Methyl-6-benzylaminomethylpiperidine. Three g of the benzylamide of 6-methylpipecolinic acid was reduced for 40 hours with 0.61 g of lithium aluminum hydride in 110 ml of a mixture of ether and benzene (1 : 1). We obtained 2.05 g (73%) of an oily, straw yellow substance, which was soluble in the usual organic solvents and insoluble in water. The b. p. was 121-122° (0.1 mm).

Found %: C 76.81; H 9.82; N 12.48. $C_{14}H_{22}N_2$. Calculated %: C 77.00; H 10.15; N 12.85.

1,6-Dimethyl-2-benzylmethylaminomethylpiperidine. A mixture of 1.85 g of 2-methyl-6-benzylaminomethylpiperidine, 2.6 ml of water, 1.64 g of 33.5% formalin solution and 2.92 g of formic acid was heated for 15 hours on a boiling water bath. The cooled solution was treated with excess of 50% potassium carbonate and extracted with ether. After drying the ether extract and distilling off the solvent we distilled the residue. We obtained 1.46 g (69.8%) of a colorless, oily substance with b. p. 128-130° (0.25 mm). The substance was soluble in the usual organic solvents and insoluble in water.

Found %: C 78.00, 77.95; H 10.19, 10.32; N 11.28, 11.25. $C_{16}H_{26}N_2$. Calculated %: C 77.99; H 10.63; N 11.37.

(Pyridyl-2')-amide of 6-methylpicolinic acid. Four g of the ester of 6-methylpicolinic acid and 20 g of α-aminopyridine were heated for 40 hours at 180° (in the bath). After this the mass was dissolved in water, the heavy, insoluble brown oil separated off in a separating funnel, dissolved in ether, dried with sodium sulfate and distilled after evaporation of the solvent. We obtained 2.44 g (47%) of a substance with b. p. 153° (0.35 mm), which was readily soluble in the usual organic solvents and insoluble in water.

Found %: C 67.47; H 5.31; N 19.79. $C_{12}H_{11}ON_3$. Calculated %: C 67.64; H 5.20; N 19.70.

2-Methyl-6-(piperidyl-2')-aminomethylpyridine. 2.12 g of the (pyridyl-2')-amide of 6-methylpicolinic acid was reduced for 20 hours with 0.56 g of lithium aluminum hydride in 55 ml of absolute ether. We obtained 0.70 g (35%) of a substance, which was soluble in the usual organic solvents and in water.

Found %: N 71.95; H 7.55; C 21.24. $C_{12}H_{13}N_3$. Calculated %: C 72.33; H 6.57; N 21.09.

Diethylaminoethylamide of 1,6-dimethylpipecolinic acid. 5 g of ethyl 1,6-dimethylpipecolinate [1] and 17.5 g of diethylaminoethylamine was heated for 40 hours so that the mixture boiled gently. The excess diethylaminoethylamine was distilled off and the residue vacuum distilled. We obtained 4.03 g (58%) of a light yellow, oily substance with b. p. 165-167° (6 mm).

Found %: N 16.63, 16.78. $C_{14}H_{29}ON_3$. Calculated %: N 16.45.

1,6-Dimethyl-2-(diethylaminoethylaminomethyl)-piperidine. Four g of the diethylaminoethylamide of 1,6-dimethylpipecolinic acid was reduced for 20 hours with 1.26 g of lithium aluminum hydride in 80 ml of absolute ether. We obtained 2.8 g (74%) of a substance with b. p. 125-127° (5 mm), which was soluble in the usual organic solvents and in water.

Found %: N 17.27, 17.66. $C_{14}H_{31}N_3$. Calculated %: N 17.40.

SUMMARY

1. Starting with lutidine, a series of substituted pyridine and piperidine amides and amines were synthesized.

2. In contrast to piperidinecarboxylic amides, pyridinecarboxylic amides were difficult to reduce with lithium aluminum hydride to the corresponding amines.

3. Pharmacological investigation showed that of the substances synthesized, only 1,6-dimethyl-2-(diethylaminoethylaminomethyl)-piperidine had a high ganglioblocking activity.

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Received January 7, 1957

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF RACEMIC METHYL ETHER OF O,O-DIBENZYLMAGNOLINE

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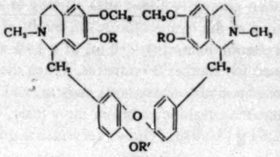
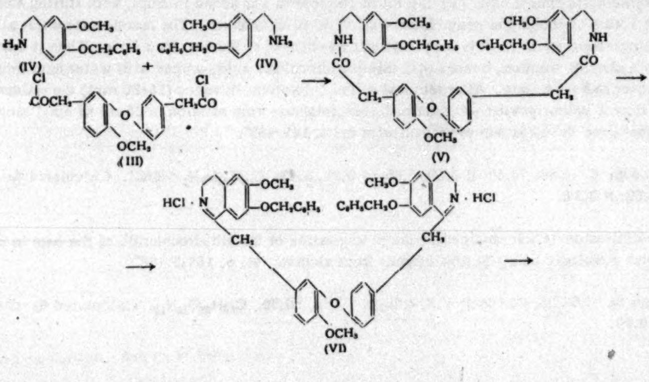
and N. A. Preobrazhenskii

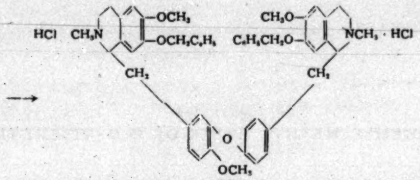
The alkaloid magnoline (I, R = R' = H) was isolated together with magnolamine by N. F. Proskurnina and A. P. Orekhov [1] in 1938 from the leaves of the Caucasian magnolia (Magnolia fusata of the family Magnoliaceae). The structure of magnoline was established by the oxidative decomposition of its trimethyl ether [2] (I, R = R' = CH_3). Here the following compounds were isolated: 1-oxo-6,7-dimethoxy-2-methyl-tetrahydroisoquinoline and 2- methoxy-4',5-dicarboxydiphenyl ether. The position of the free hydroxyl groups was established by the oxidation of the triethyl ether of the alkaloid. On the basis of the performed studies the following formula was proposed for magnoline (I, R = R' = H).


OCH₃
CH₃O
CH₃–N
OR
RO
N–CH₃
CH₂
CH₂
O
OR'

(I)

We synthesized the dihydrochloride of 2-methoxy-4',5-bis-(6-methoxy-7-benzyloxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolylmethyl)-diphenyl ether (II), which after removal of the benzyl radicals can be converted into the (±) methyl ether of magnoline (I, R = H, R' = CH_3).


H₂N
OCH₃
OCH₂C₆H₅
(IV)
CH₃O
C₆H₅CH₂O
NH₂
(IV)
+
Cl
COCH₂
O
OCH₃
(III)
Cl
CH₂CO
NH
CO
OCH₃
OCH₂C₆H₅
CH₃O
C₆H₅CH₂O
NH
CO
CH₂
O
CH₂
OCH₃
(V)
HCl · N
OCH₃
OCH₂C₆H₅
CH₃O
C₆H₅CH₂O
N · HCl
CH₂
CH₂
O
OCH₃
(VI)



(II)

The starting compounds for the synthesis were the dichloride of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether [3] (III) and 3-methoxy-4-benzyloxyphenethylamine (IV), which when reacted with each other in the presence of potash gave diamide (V). The latter when reacted with phosphorus pentachloride was converted to the bisdihydroisoquinoline derivative (VI), which was then subjected to catalytic hydrogenation, followed by methylation with formalin in the presence of formic acid.

EXPERIMENTAL

Bis(3-methoxy-4-benzyloxyphenethylamide) of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether (V). A mixture of 1.3 g of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether and 4.86 g of thionyl chloride was heated at 50-60° for 2 hours. The excess thionyl chloride was vacuum-distilled, and the residue was dissolved in 30 ml of chloroform. The latter was then gradually added with stirring to a solution of 3-methoxy-4-benzyloxyphenethylamine (isolated from 3.61 g of the hydrochloride) in 50 ml of chloroform. At the same time, maintaining a weakly alkaline medium (phenolphthalein), 6-8 ml of a 10% aqueous solution of potassium carbonate was added. The stirring was continued for another 30 minutes. Then the chloroform layer was separated, washed with 5% hydrochloric acid solution, then with water until neutral, and dried over sodium sulfate. After removal of the solvent in vacuo (15-20 mm) the residue, a brown tarry mass, was rubbed in ether. Here a powder with m. p. 94-96° was obtained. Yield 2.64 g (80.8%). Three recrystallizations from ethyl alcohol gave colorless crystals with m. p. 109-110°.

Found %: C 73.88, 74.12; H 6.65, 6.57; N 3.80, 3.53. $C_{49}H_{50}O_8N_2$. Calculated %: C 74.03; H 6.35; N 3.52.

2-Methoxy-4',5-bis(6-methoxy-7-benzyloxy-3,4-dihydro-1-isoquinolylmethyl)diphenyl ether dihydrochloride (VI). To a solution of 1.3 g of the bis(3-methoxy-4-benzyloxyphenethylamide) of 2-methoxy-4',5-bis(carboxymethyl)diphenyl ether (V) in 8 ml of chloroform was added in drops, with stirring and cooling, a solution of 1.49 g of phosphorus pentachloride in 36 ml of chloroform. The reaction mass was allowed to stand at room temperature for three days, and finally it was heated at the boil for 1 hour. Then it was washed with 2% sodium hydroxide solution, treated with dilute hydrochloric acid, washed with water until neutral (to Congo) and dried over sodium sulfate. After removal of the chloroform in vacuo (15-20 mm) the residue was rubbed in ether. Here a yellow powder was obtained. Precipitation from solution in 25 ml of ethyl alcohol with anhydrous ether gave 0.7 g (51.3%) of product with m. p. 147-153°.

Found %: C 70.86, 70.50; H 5.59, 5.65; N 3.71, 3.43. $C_{49}H_{46}O_6N_2 \cdot 2HCl$. Calculated %: C 70.75; H 5.82; N 3.37.

The dipicrolonate was obtained by the precipitation of the dihydrochloride of the base in chloroform solution with picrolonic acid. Yellow crystals from alcohol. M. p. 167.5-168°.

Found %: C 64.06, 64.12; H 5.18, 4.98; N 10.64, 10.79. $C_{69}H_{62}O_{16}N_{10}$. Calculated %: C 64.38; H 4.86; N 10.90.

2-Methoxy-4',5-bis(6-methoxy-7-benzyloxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolylmethyl)diphenyl ether dihydrochloride (II). A solution of 0.22 g of the dihydrochloride of 2-methoxy-4',5-bis(6-methoxy-7-benzyloxy-3,4-dihydro-1-isoquinolylmethyl)diphenyl ether (VI) in 20 ml of anhydrous ethyl alcohol was filtered and then hydrogenated over platinum catalyst (from 0.3 g of platinum oxide) with constant shaking for 5 hours at room temperature. The catalyst was removed, while the alcohol was vacuum-distilled (15-20 mm) in a stream of nitrogen. The residue was dissolved in 40 ml of chloroform, shaken with 10% sodium carbonate solution, washed with water until neutral (phenolphthalein), and the solvent removed by vacuum-distillation (15-20 mm). To the residue was added 0.06 ml of 38.4% formalin and 0.17 ml of 88% formic acid, and the whole heated for 5 hours on the water bath. Then 15-20 ml of benzene was added, and 5% sodium hydroxide solution until alkaline. The substance was extracted from the water layer with benzene; the combined extracts were washed with water and dried over sodium sulfate. After filtration, the solution was treated with benzene, saturated with hydrogen chloride. The nearly colorless precipitate was washed by decantation with ether until neutral (to Congo) and then dried. Yield 0.083 g (35%).

Found %: C 68.76; H 6.75; N 3.12. $C_{51}H_{54}N_2O_6 \cdot 2HCl \cdot 1\,{}^1/_2H_2O$. Calculated %: C 68.75; H 6.68; N 3.14.

Nearly colorless crystals were obtained after drying in vacuo (3 mm) for 2 hours at 60°. M. p. 136-138°.

Found %: C 70.76, 70.72; H 6.37, 6.36; N 3.15. $C_{51}H_{54}N_2O_6 \cdot 2HCl$. Calculated %: C 70.90; H 6.53; N 3.24.

SUMMARY

The racemic methyl ether of O,O-dibenzylmagnoline was synthesized.

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Received November 24, 1956

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*Original Russian pagination. See C. B. Translation.

DIENE HYDROCARBONS FROM UNSATURATED ALCOHOLS

I. CATALYTIC DEHYDRATION OF CROTYL ALCOHOL TO BUTADIENE

Iu. A. Gorin, V. S. Ivanov, E. S. Bogdanova and E. A. Plaivinen

Diene hydrocarbons with a conjugated system of double bonds can be obtained by the catalytic dehydration of α, β-unsaturated alcohols. The dehydration of crotyl alcohol yields butadiene. As catalysts for the dehydration of crotyl alcohol various authors used toluidine bisulfate, anhydrous oxalic acid, $KHSO_4$, H_3PO_4, $AlCl_3$ [1], kaolin, $AlPO_4$ [2], precipitated Al_2O_3, [3], and the mixed catalysts kaolin$-H_3PO_4$ and kaolin$-Fe_2O_3-KOH$ [4]. The yields of butadiene using the indicated catalysts ranged from 25 to 57 mole %, based on passed (taken) alcohol. Iu. A. Gorin [5] investigated the transformations of crotyl alcohol on one of the dehydrating components of the S. V. Lebedev catalyst. The highest yield of butadiene was obtained at 325° (54.2 mole %, based on passed alcohol). According to the studies of the American authors [6], the yield of butadiene from crotyl alcohol over silica gel can reach 75% at 350°. To explain the formation of butadiene from ethyl alcohol by the S. V. Lebedev method, Iu. A. Gorin [7] proposed a scheme in which crotyl alcohol was regarded as being an unstable intermediate product, the dehydration of which gave butadiene. Since the yield of butadiene from ethyl alcohol is very high by the S. V. Lebedev method, then it is obvious that the intermediate stage in its formation—the dehydration of crotyl alcohol—should also proceed with high yield.

In the present investigation we studied the dehydration of crotyl alcohol under conditions close to those of the S. V. Lebedev process. For this we used the various dehydrating components of the S. V. Lebedev catalyst, which made it possible to mold the process to some degree in its last stage—the formation of butadiene by the dehydration of crotyl alcohol. In addition, a study of the transformations of crotyl alcohol over certain dehydrating catalysts under various conditions had as one of its problems the selection of the most effective contacts for the dehydration of crotyl alcohol with the purpose of obtaining butadiene from it in high yield. It seemed of interest to first make a thermodynamical calculation of the reaction for the dehydration of crotyl alcohol in order to determine if its accomplishment was practically feasible. Data on the free energy, heat content, entropy and change in the heat capacity as a function of the temperature are absent for crotyl alcohol. For this reason we limited ourselves to an approximate calculation, using the method based on the additivity of thermodynamic functions for organic molecules.

The reaction is run at temperatures above the boiling point of crotyl alcohol (i.e., above 120°), and consequently proceeds in the gas phase ($\Delta\nu = 1$). Using the data of Bremner and Thomas [8] for the values of the normal free energies of alcohol groups, calculated for a number of temperatures, we calculated the free energy of crotyl alcohol at 300, 600 and 800°K (Table 1). Calculated in this manner, the free energy of formation of crotyl alcohol at 300°K ($\Delta F = -16{,}000$ cal/mole) is found to be in agreement with the results obtained by us using other calculation methods, also based on the property of additivity: $\Delta F_s = -15{,}000$ cal/mole [9], and $\Delta F_s = -16{,}610$ and $-16{,}760$ cal/mole [10]. When the calculation is made starting from liquid primary n-butyl alcohol with its conversion to a gas, followed by dehydration, the value obtained for $\Delta F_s = -16{,}575$ kcal/mole.

Calculation of the change in the free energy of the dehydration reaction makes it possible to determine the equilibrium constants K_p and the yields of butadiene. The values of the free energies for crotyl alcohol, butadiene, water and the reaction for the dehydration of crotyl alcohol, the equilibrium constants K_p, and the yields of butadiene, calculated for 300, 600 and 800°K, are given in Table 1, from which it can be seen that even at 27° (300°K) it is theoretically possible for the reaction to go nearly to completion. The yield increases as the temperature is increased.

TABLE 1

Approximate Thermodynamic Calculation of the Reaction for the Dehydration of Crotyl Alcohol

T (°K)	ΔF (kcal/mole) crotyl alcohol	butadiene [11]	water [11]	Free energies (kcal/mole)	K_p	Yield C_4H_6 (mole %)
300	−16.00	36.49	−54.62	−2.13	36	97.1
600	+7.00	47.21	−51.16	−10.95	9816	~100
800	22.50	54.92	−48.65	−16.23	27350	~100

It should be mentioned that thermodynamic considerations alone cannot serve as a criterion in investigating a chemical reaction. Thermodynamic data should be regarded in association with the chemical peculiarities of the process. In the present case the use of vacuum facilitates a more complete conversion of crotyl alcohol into butadiene, while raising the temperature facilitates this only up to a certain limit, after which the yields of butadiene will decrease due to intensification of secondary processes.

In the present study on the dehydration of crotyl alcohol we investigated the following catalysts: 1) the various dehydrating components of the S. V. Lebedev catalyst—B, B_1, B_2, B_3 and B_4; 2) a complex phosphate catalyst, used by the synthetic rubber industry in Germany for the dehydration of 1,3-butylene glycol to butadiene [12]—F; 3) a calcium phosphate catalyst having the composition: 70% $Ca_3(PO_4)_2$ + 30% $CaHPO_4$ − F_{Ca}; 4) anhydrous magnesium sulfate, the use of which for the dehydration of some α, β-unsaturated alcohols is indicated by D. V. Tishchenko [13], − $MgSO_4$; 5) magnesium sulfate, deposited on silica gel−$MgSO_4$-2; 6) activated aluminum oxide−AOA; 7) silica gel−SiO_2; and 8) silica gel-tantalum catalyst, used in U.S.A. for the preparation of butadiene from a mixture of ethyl alcohol and acetaldehyde−98% SiO_2 + Ta_2O_5 [14].

The results obtained by us in the dehydration of crotyl alcohol over the various catalysts are summarized in Tables 2 and 3.

The results of the experiments on the converison of crotyl alcohol over the various dehydrating components of the S. V. Lebedev catalyst and over some of the phosphate catalysts are given in Table 2.

From the data in Table 2 it follows that using component B makes it possible to obtain substantial yields of butadiene from crotyl alcohol, reaching values as high as 88.5 mole %, based on alcohol passed through. The use of catalyst B_2 creates conditions similar to those that prevail in the process for the preparation of butadiene from ethyl alcohol, where crotyl alcohol is the intermediate product. The fact that butadiene is formed in such high yield in this case indicates that the intermediate stage of the formation and dehydration of crotyl alcohol does not serve to impede progress of the S. V. Lebedev process. Liquid products were obtained together with butadiene when catalyst B_2 was used, which were found to contain methylvinylcarbinol, formed as the result of allylic rearrangement of the crotyl alcohol. For catalysts of the B type the optimum temperature for the decomposition of crotyl alcohol proved to be 350°.

The gaseous products obtained when the complex phosphate catalyst F was used were found to contain nearly pure butadiene, the yield of the latter reaching 82 mole %. The gas from the experiments with calcium phosphate was also rich in butadiene, but the yields of the latter were lower.

The experimental data on the dehydration of crotyl alcohol over magnesium sulfate, activated aluminum oxide, and silica gel in a mixture of silica gel with tantalum pentoxide, are presented in Table 3. The maximum yields of butadiene were obtained using magnesium sulfate deposited on silica gel ($MgSO_4$-2). The use of activated aluminum oxide gave a much lower yield of butadiene than that obtained with the other catalysts. Here the process for the dehydration of crotyl alcohol is complicated by side reactions, as evidenced by the greater amount of butylenes in the gas (up to 34 volume %). The formation of butylenes can be explained by stating that crotyl alcohol under the influence of aluminum oxide is partially isomerized to butyraldehyde, which is then reduced by the crotyl alcohol to butyl alcohol. The dehydration of the latter yields butylenes.

TABLE 2

Catalytic Dehydration of Crotyl Alcohol Over Various Dehydrating Components of the S. V. Lebedev Catalyst and Over Phosphate Catalysts

Expt. No.	Catalyst	Expt. temp., (°C)	Admittance (ml/hr/ml catalyst)	Diluent and degree of dilution (mole)	Alcohol passed (g)	Air-free gas (l stand. conditions)	Composition of gas (volume %)							C_4H_6 on alcohol passed (mole %)
							CO_2	$C_4H_8+C_3H_6$	C_2H_4	CO	H_2	CH_4	C_4H_6	
1	B	325°	0.69	—	4.25	0.87	2.9	11.7	0.6	0.0	0.0	2.1	82.9	55.9
2	B	350	0.69	—	4.25	0.93	1.5	9.9	1.0	0.0	0.0	1.5	86.1	62.1
3	B	375	0.69	—	4.25	0.82	1.8	23.6	1.3	0.0	0.0	1.2	72.2	48.3
4	B_1	350	0.58	—	4.25	1.08	2.4	1.9	2.4	0.0	0.8	1.1	91.3	77.0
5	B_2	350	0.58	—	4.25	1.16	1.5	0.0	1.8	0.0	0.0	2.3	94.5	85.0
6	B_3	350	0.58	—	4.25	1.09	3.0	0.0	1.0	0.0	0.0	0.5	95.5	80.5
7*	B_2	350	0.60	N 1 : 1	4.25	1.20	1.7	0.0	0.0	0.0	0.0	4.3	94.1	86.6
8*	B_2	350	0.60	N 1 : 3.5	4.25	1.20	1.2	0.0	0.0	0.0	0.0	2.8	96.0	87.6
9	B_2	350	0.60	H_2O: 1 : 13	4.25	1.20	2.4	0.3	1.0	0.0	0.0	1.3	95.0	88.5
10	B_4	350	0.60	—	3.67	0.81	5.3	0.5	1.1	0.7	0.0	1.6	90.5	61.4
11*	B_4	350	0.60	N 1 : 3.5	3.26	0.83	6.1	0.0	0.7	0.4	1.7	4.4	88.5	74.1
12	F	270	0.21	—	4.25	1.08	2.1	0.0	0.8	0.0	1.0	0.0	96.1	81.8
13	F_{Ca}	305	0.70	H_2O; 1 : 10	4.08	0.84	4.6	1.7	1.2	0.5	0.0	—	93.5	63.6
14	F_{Ca}	330	0.70	H_2O 1 : 10	3.26	0.64	7.6	0.0	1.1	0.5	—	—	91.1	58.9
15	F_{Ca}	425	0.70	H_2O 1 : 10	4.08	0.82	3.4	1.7	2.7	0.2	3.4	—	88.5	58.8

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*In Expt. Nos. 7, 8 and 11 the volume of nitrogen-free gas was considered.

$$CH_3{-}CH{=}CH{-}CH_2OH \rightarrow CH_3{-}CH_2{-}CH_2{-}CHO$$

$$CH_3{-}CH_2{-}CH_2{-}CHO + CH_3{-}CH{=}CH{-}CH_2OH \rightarrow CH_3{-}CH_2{-}CH_2{-}CH_2OH + \\ + CH_3{-}CH{=}CH{-}CHO$$

$$CH_3{-}CH_2{-}CH_2{-}CH_2OH \rightarrow CH_3{-}CH_2{-}CH{=}CH_2 + H_2O$$

Similar cases of the isomerization of α,β-unsaturated alcohols are described in the literature [15]. For example, allyl alcohol at 300° over aluminum oxide is converted to propionaldehyde.

$$CH_2{=}CH{-}CH_2OH \rightarrow CH_3{-}CH_2{-}CHO$$

Together with butadiene, a small amount of butylenes is also formed from crotyl alcohol when the dehydrating component B of the S. V. Lebedev catalyst is used (Table 2, Expts. 1-3). Their probable formation is explained by the scheme given above.

In contrast to the American authors [6], we failed to find any indication that silica gel is a highly active catalyst for the dehydration of crotyl alcohol. Using a mixture of silica gel and tantalum pentoxide (2% Ta_2O_5 + 98% SiO_2), the yield of butadiene in the experiments where the crotyl alcohol was diluted with nitrogen proved to be large. It is known that a silica gel-tantalum catalyst of the above indicated composition is used in the synthetic rubber industry in the U.S.A. to obtain butadiene from a mixture of ethyl alcohol and acetaldehyde [14, 16].

$$C_2H_5OH + CH_3CHO \rightarrow CH_2{=}CH{-}CH{=}CH_2 + 2H_2O$$

According to Quattlebaum [17] and some other authors [6], the reaction proceeds in two stages: 1) crotonization of the acetaldehyde $CH_3CHO + CH_3CHO \rightarrow CH_3{-}CH{=}CH{-}CHO + H_2O$ and 2) deoxidation of the crotonaldehyde by ethyl alcohol to butadiene $CH_3{-}CH{=}CH{-}CHO + CH_3CH_2OH \rightarrow CH_2{=}CH{-}CH{=}CH_2 + CH_3CHO + H_2O$.

It is possible to assume that the preparation of butadiene from crotonaldehyde proceeds in the given case through the intermediate stage of forming crotyl alcohol, i.e., not only deoxidation of the crotonaldehyde by ethyl alcohol occurs (associated with the removal of oxygen from crotonaldehyde), but also a related dehydrogenation with subsequent dehydration.

$$CH_3{-}CH{=}CH{-}CHO + CH_3CH_2OH \rightarrow CH_3{-}CH{=}CH{-}CH_2OH + CH_3CHO$$

$$CH_3{-}CH{=}CH{-}CH_2OH \rightarrow CH_2{=}CH{-}CH{=}CH_2 + H_2O$$

The results obtained by us show that when a silica gel-tantalum catalyst is used the yield of butadiene from crotyl alcohol (when the alcohol is diluted with nitrogen) is as high as 83 mole %, based on alcohol passed through. This circumstance permits the postulation that the preparation of butadiene from a mixture of ethyl alcohol and acetaldehyde on a silica gel-tantalum catalyst, the same as in the S. V. Lebedev process, can proceed through the stage of formation and subsequent dehydration of crotyl alcohol.

EXPERIMENTAL

Crotyl Alcohol was obtained by the reduction of crotonaldehyde with aluminum isopropoxide [18]; b. p. 120-121.5°, d_4^{20} 0.8502; n_D^{20} 1.4270; α-naphthylurethan, m. p. 95°.

Found %: N 5.85. $C_{15}H_{15}O_2N$. Calculated %: N 5.81.

TABLE 3

Catalytic Dehydration of Crotyl Alcohol Over Magnesium Sulfate, Aluminum Oxide and Silica Gel-Containing Catalysts

Expt. No.	Catalyst	Expt. temp. (°C)	Admittance (ml/hr/ml catalyst)	Diluent and degree of dilution (mole)	Alcohol passed (g)	Air-free gas (l, stand. conditions)	Composition of gas (volume %)							C_4H_6 on alcohol passed (mole %)
							CO_2	$C_4H_8+C_3H_6$	C_2H_4	CO	H_2	CH_4	C_4H_6	
1	$MgSO_4$	230°	0.28	—	4.08	0.53	3.2	2.4	1.5	0.7	1.2	—	91.2	39.2
2	$MgSO_4$	260	0.28	—	4.03	0.84	3.6	1.5	1.3	0.6	0.0	2.9	90.5	61.5
3	$MgSO_4$	285	0.28	—	4.08	0.73	5.1	0.5	1.4	0.7	2.1	—	87.0	51.5
4	$MgSO_4$—2	270	0.45	—	4.08	0.85	6.9	0.0	1.2	0.2	0.0	0.0	93.2	64.2
5*	$MgSO_4$—2	270	0.45	N 1 : 3	4.03	1.03	2.1	1.7	1.6	0.0	0.0	0.0	92.5	77.1
6*	$MgSO_4$—2	300	0.45	N 1 : 3	4.08	1.09	1.7	0.8	1.5	0.0	1.3	0.0	93.9	82.8
7*	$MgSO_4$—2	330	0.45	N 1 : 3	4.08	1.09	1.3	1.3	0.9	0.4	0.0	0.0	96.0	84.8
8	AOA (NIUIF)**	380	0.56	—	4.08	0.77	4.8	19.0	2.6	1.4	0.4	2.4	66.0	41.2
9	AOA (Dneprodzerzhinsk)	380	0.53	—	4.08	0.68	4.1	34.3	0.0	1.5	4.1	2.3	50.1	27.6
10	SiO_2	350	0.53	—	4.25	0.35	1.6	0.0	1.6	0.0	0.0	2.8	94.0	25.7
11	SiO_2	375	0.51	—	4.25	0.32	0.0	0.0	1.0	0.0	0.0	3.0	96.0	23.8
12	$SiO_2+Ta_2O_5$	350	0.53	—	4.08	0.81	0.9	4.4	1.2	0.0	1.3	2.8	87.6	57.5
13	$SiO_2+Ta_2O_5$	370	0.53	—	4.08	0.86	1,4	8.9	1.9	0.2	0.8	3.1	83.6	58.2
14*	$SiO_2+Ta_2O_5$	370	0.53	N 1 : 3	4.08	1.12	3.6	2.2	0.7	0.0	0.0	1.1	91.8	83.3

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*In Expt. Nos. 5-7 and 14 the volume of nitrogen-free gas was considered.

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According to the literature data for crotyl alcohol: b. p. 121.5-122°, d_4^{20} 0.8490, n_D^{20} 1.42591 [19]; for α-naphthylurethan: m. p. 91-93° [6].

Apparatus and Method of Operation. The experiments on the dehydration of crotyl alcohol were run using a small laboratory catalysis apparatus. A quantz tube, containing 26 ml of catalyst, was inserted into a vertical catalysis furnace 25 cm high. A layer of fine quartz, serving as the vaporizer, was sifted over the catalyst layer. First it was established that crotyl alcohol is not decomposed on quartz under the experimental conditions used. To measure the temperature in the reaction zone the hot junction of a chromel-alumel thermocouple was placed in the center of the catalyst in the quartz container. A special apparatus, described earlier [20], was used to add the alcohol at a uniform rate from the injector.

In the experiments where the crotyl alcohol was diluted with water the latter was fed from a separate dropping device, while when nitrogen was used for dilution the rate of its passage was regulated using a rheometer. The liquid reaction products were condensed using condensers and then collected in an ice-cooled receiver. The gas was collected in a gasholder over saturated sodium chloride solution. After completing the passage of crotyl alcohol, water (about 3-5 ml) was fed into the furnace to displace the reaction products. The gaseous products were analyzed using the apparatus designed by VTI (All-Union Heat Engineering Institute). The amount of butadiene in the gas was determined by bromination (based on the weight of tetrabromobutane) and by the amount of maleic anhydride adduct. The tetrabromide of butadiene after recrystallization from alcohol had m. p. 117°. According to [21]: m. p. 118°.

The results of the catalytic conversion of crotyl alcohol are summarized in Tables 2 and 3.

Using the dehydrating component B_2 of the S. V. Lebedev catalyst, which favors the formation of butadiene from crotyl alcohol in maximum yield, we ran a series of experiments at 350° in order to accumulate and study the liquid conversion products. The experiments were run with a passage rate of 10 ml/hour/ml catalyst. A total of 102 g of crotyl alcohol was passed through. The obtained condensate consisted of two layers. Distillation of the lower water layer gave a fraction with b. p. 82-98°. The distillate was salted out with potash. The separated upper layer was added to the upper layer of the condensate, and the mixture was dried over potash. The dried product (42.26 g) was fractionated through a rectification column into the following fractions: 1st b. p. 76-87°, 2.33 g; 2nd b. p. 87-94°, 0.64 g, n_D^{20} 1.4110; 3rd b. p. 94-98°, 3.56 g, n_D^{20} 1.4181; 4th b. p. 98-118°, 2.21 g, n_D^{20} 1.4249, 5th b. p. 118-121°, 18.40 g, n_D^{20} 1.4282, residue and losses, 15.11 g.

The main portion of fraction 3 (94-98°, d_4^{20} 0.8329) distilled at 96.5°, which corresponds to methylvinylcarbinol. Literature data for methylvinylcarbinol: b. p. 97.2-97.3°, d_4^{20} 0.8318, n_D^{20} 1.4127 [19]. Treatment of the fraction with b. p. 94-98° with α-naphthyl isocyanate gave the urethan, which after recrystallization from petroleum ether was obtained as fine, pale yellow needle crystals with m. p. 93.5°. The mixed melting point with the α-naphthylurethan of crotyl alcohol was strongly depressed (69°). The amount of nitrogen in the obtained α-naphthylurethan was determined by Dumas microanalysis.

Found %: N 5.81. $C_{15}H_{15}O_2N$. Calculated %: N 5.81.

Information on the melting point of the α-naphthylurethan of methylvinylcarbinol is absent in the literature. Due to this we dehydrated 1,3-butylene glycol [22] to yield methylvinylcarbinol (b. p. 96-98°, d_4^{20} 0.8381, n_D^{20} 1.4120) and then prepared the α-naphthylurethan from it with m. p. 94°. The mixture of α-naphthylurethans, obtained from methylvinylcarbinol and from the fraction with b. p. 94-98°, melted at 93.5°.

The 5th fraction corresponds to unreacted crotyl alcohol.

In another portion of the crude condensate, after drying over fused $CuSO_4$, the amount of carbonyl compounds was determined quantitatively by the use of hydroxylamine hydrochloride. The amount of carbonyl compounds, calculated on the basis of C_4H_6O (either crotonaldehyde or methyl vinyl ketone, the presence of which is the most probable), was 0.12%.

SUMMARY

1. The equilibrium constants of the reaction for the dehydration of crotyl alcohol to butadiene were calculated, and from them the yields of reaction products in the temperature interval 300-800°K. From an approximate thermodynamic calculation it follows that thermodynamic limitations do not exist for the given

reaction. The yield of butadiene from crotyl alcohol increases when the temperature is raised and reduced pressure is employed.

2. A number of catalysts for the dehydration of crotyl alcohol to butadiene were examined. The best results were obtained using one of the dehydrating components, namely B_2, of the S. V. Lebedev catalyst, and here the yield of butadiene was 85-88.5 mole %, based on alcohol passed through.

3. The liquid products obtained in the catalytic dehydration of crotyl alcohol over catalyst B_2 were found to contain methylvinylcarbinol, formed as the result of crotyl alcohol isomerization.

4. The obtained results agree with the ideas regarding the scheme for the formation of butadiene from ethyl alcohol by the S. V. Lebedev method, according to which crotyl alcohol is an intermediate product in this process.

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Received December 30, 1956

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*Original Russian pagination. See C. B. Translation.

REACTION OF ALKYLENE SULFIDES WITH HALIDES OF CARBOXYLIC ACIDS

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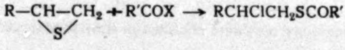
The reaction of alkylene sulfides with the halides of carboxylic acids has been studied but slightly up to now. It was only quite recently that studies were made of the reaction of ethylene sulfide with the chlorides of some aliphatic and aromatic carboxylic acids [1-3].

We studied the reaction of ethylene sulfide and of propylene sulfide with acetyl bromide, acetyl iodide, with the chlorides of mono-, di- and trichloroacetic acids, and with the bromides and iodides of other acids.

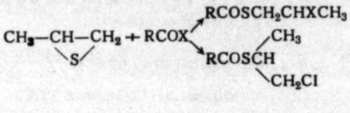
Acyl halides readily add to alkylene sulfides with the formation of the corresponding 2-haloalkyl thiolcarboxylates



The acyl chlorides add at a slower rate than do the corresponding bromides and iodides. Thus, if the chlorides add to alkylene sulfides when the reactants are mixed and heating is required to complete the reaction, then when the bromides, and especially the iodides, are added to alkylene sulfides the reaction proceeds so vigorously that cooling is required. For this reason the addition of the carboxylic acid bromides and iodides to alkylene sulfides was made in dry carbon tetrachloride medium and with cooling. Here reaction was practically complete immediately after all of the alkylene sulfide had been added to the acid halide.

It should also be mentioned that the longer the hydrocarbon chain of the acid halide, the slower the reaction with the alkylene sulfide and the smaller the yield of the corresponding 2-haloalkyl thioester.

The reaction of propylene sulfide with acid halides can proceed in two directions to yield either the 2-halo-n-propyl thioester (I) or the 2-halo-isopropyl thioester (II).



(I)

(II)

The direction of this reaction was studied on the example of adding acetyl iodide to propylene sulfide.

To determine the direction of the reaction we used the method of comparing the melting point of the crystalline derivative of the product obtained from the reaction of propylene sulfide with acetyl iodide with that of the corresponding compound of known structure.

To obtain the crystalline derivative we added the reaction product of propylene sulfide with acetyl iodide to trimethylamine

$$(CH_3)_3N + CH_3COSC_3H_6I \longrightarrow (CH_3)_3\overset{+}{\underset{\bar{I}}{N}}{-}C_3H_6SCOCH_3$$

The 2-(acetothio)propyltrimethylammonium iodide obtained in this manner had m. p. 234°.

Acetyl β-methylthiocholine iodide $(CH_3)_3\underset{I}{\overset{+}{N}}-CH_2CH(CH_3)SCOCH_3$, synthesized by the Renshaw method [4], has m. p. 144-145°. Its mixture with the 2-(acetothio)propyltrimethylammonium iodide obtained by us melted at 131°, i.e., it gave a sharp depression.

As a result, the obtained substance proved to be different from acetyl β-methylthiocholine iodide. It should have only one possible structure, namely that of acetyl α-methylthiocholine iodide $(CH_3)_3\underset{I}{\overset{+}{N}}-CH(CH_3)-CH_2SCOCH_3$. The formation of a substance with such a structure is possible if propylene sulfide is cleaved by acetyl iodide according to direction (I) with the formation of 2-iodo-n-propyl thiolacetate.

EXPERIMENTAL

Preparation of 2-Chloroethyl Trichlorothiolacetate. Three grams of ethylene sulfide was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Nine grams of trichloroacetyl chloride was gradually added from the dropping funnel to the alkylene sulfide at the boil. After all of the chloride had been added the reaction mixture was heated at 60° for 1.5 hours. The obtained 2-chloroethyl trichlorothiolacetate was vacuum-distilled. Yield 9 g (75%).

B. p. 88-89° (3 mm), d_4^{17} 1.5492, n_D^{17} 1.5351. MR_D 48.41; calc. 48.29.

Found %: Cl 58.21; S 12.97. $C_4H_4OCl_4S$. Calculated %: Cl 58.00; S 13.26.

The other 2-chloroalkyl thiolcarboxylates were obtained in similar manner.

Preparation of 2-chloropropyl chlorothiolacetate. For reaction we took 11.3 g of chloroacetyl chloride and 7.4 g of propylene sulfide. We obtained 12.4 g (67%) of compound.

B. p. 85° (2.5 mm), d_4^{18} 1.3125, n_D^{18} 1.5201, MR_D 43.35; calc. 43.00.

Found %: Cl 38.06; S 16.58. $C_5H_8OCl_2S$. Calculated %: Cl 37.99; S 17.16.

Preparation of 2-chloropropyl dichlorothiolacetate. For reaction we took 5 g of propylene sulfide and 7 g of dichloroacetyl chloride. We obtained 7 g (63%) of compound.

B. p. 90° (2 mm), d_4^{18} 1.3651, n_D^{18} 1.4995, MR_D 47.50; calc. 49.94.

Found %: Cl 47.53; S 14.40. $C_5H_7OCl_3S$. Calculated %: Cl 48.02; S 14.51.

Preparation of 2-chloropropyl trichlorothiolacetate. For reaction we took 5 g of propylene sulfide and 8 g of trichloroacetyl chloride. We obtained 7.6 g (67%) of compound.

B. p. 95° (2 mm), d_4^{18} 1.4345, n_D^{18} 1.5048, MR_D 52.206; calc. 52.834.

Found %: Cl 54.75; S 12.78. $C_5H_6OCl_4S$. Calculated %: Cl 55.38; S 12.52.

Preparation of 2-bromoethyl thiolacetate. A mixture of 20 g of acetyl bromide and 30 ml of dry carbon tetrachloride was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Then, with water-cooling, 10.5 g of ethylene sulfide was added gradually from the dropping funnel. After all of the sulfide had been added the reaction mixture was heated at 60° for 20 minutes, the solvent removed by distillation, and the 2-bromoethyl thiolacetate vacuum-distilled. Yield 21 g (70%).

B. p. 78° (10 mm), d_4^{19} 1.5330, n_D^{19} 1.5220, MR_D 36.20; calc. 36.22.

Found %: Br 44.0; S 17.20. C_4H_7OBrS. Calculated %: Br 43.7; S 17.50.

The other 2-haloalkyl thiolcarboxylates were obtained in similar manner.

Preparation of 2-bromoethyl bromothiolacetate. For reaction we took 12 g of bromoacetyl bromide, twenty ml of carbon tetrachloride and 3.6 g of ethylene sulfide. We obtained 10 g (64.5%) of substance with b. p. 117° (5 mm), d^{21}_{D} 1.928.

Found %: Br 61.40; S 12.00. $C_4H_6OBr_2S$. Calculated %: Br 61.10; S 12.20.

Preparation of 2-bromoethyl thiolpropionate. For reaction we took 7 g of propionyl bromide, 15 ml of carbon tetrachloride and 3 g of ethylene sulfide. We obtained 9 g (90%) of 2-bromoethyl thiolpropionate.

B. p. 97° (16 mm), d^{17}_{4} 1.4285, n^{17}_{D} 1.5220, MR_D 41.60; calc. 40.87.

Found %: Br 40.82; S 16.03. C_5H_9OBrS. Calculated %: Br 40.6; S 16.25.

Preparation of 2-bromoethyl thiolbutyrate. For reaction we took 15.1 g of butyryl bromide, 25 ml of carbon tetrachloride and 6 g of ethylene sulfide. We obtained 16 g (76%) of 2-bromoethyl thiolbutyrate.

B. p. 102° (13 mm), d^{20}_{4} 1.3294, n^{20}_{D} 1.500. MR_D 46.38; calc. 45.48.

Found %: Br 38.15; S 14.86. $C_6H_{11}OBrS$. Calculated %: Br 37.9; S 15.14.

Preparation of 2-bromoethyl thiolbenzoate. For reaction we took 9 g of benzoyl bromide, 10 ml of carbon tetrachloride and 2.9 g of ethylene sulfide. We obtained 6.5 g (54.6%) of 2-bromoethyl thiolbenzoate with b. p. 153° (13 mm) (partial decomposition) and d^{19}_{4} 1.4850.

Found %: Br 32.88; S 12.87. C_9H_9OBrS. Calculated %: Br 32.63; S 13.05.

Preparation of 2-bromopropyl thiolacetate. For reaction we took 6.7 g of acetyl bromide, 15 ml of carbon tetrachloride and 4 g of propylene sulfide. We obtained 10 g (85%) of 2-bromopropyl thiolacetate.

B. p. 58° (3 mm), d^{10}_{4} 1.4220, n^{10}_{D} 1.5110, MR_D 41.40; calc. 40.87.

Found %: Br 40.81; S 16.00. C_5H_9OBrS. Calculated %: Br 40.6; S 16.25.

Preparation of 2-iodopropyl thiolacetate. For reaction we took 14 g of acetyl iodide, 20 ml of carbon tetrachloride and 6.1 g of propylene sulfide. We isolated 14.2 g (70.5%) of 2-iodopropyl thiolacetate.

B. p. 85° (8 mm), d^{22}_{4} 1.5465, n^{22}_{D} 1.5030, MR_D 44.10; calc. 45.10.

Found %: I 52.15, S 12.95. C_5H_9OIS. Calculated %: I 52.00; S 13.12.

Preparation of 2-bromopropyl bromothiolacetate. For reaction we took 12 g of bromoacetyl bromide, 30 ml of carbon tetrachloride and 4.4 g of propylene sulfide. We obtained 8 g (48.8%) of 2-brompropyl bromothiolacetate with b. p. 124° (7 mm), d^{20}_{4} 1.7560.

Found %: Br 58.20; S 11.45. $C_5H_8OBr_2S$. Calculated %: Br 57.91; S 11.6.

Preparation of 2-bromopropyl thiolpropionate. For reaction we took 7 g of propionyl bromide, 10 ml of carbon tetrachloride and 4 g of propylene sulfide. We isolated 8 g (72.5%) of 2-bromopropyl thiolpropionate.

B. p. 100° (15 mm), d^{20}_{4} 1.3425, n^{20}_{D} 1.5010, MR_D 46.35; calc. 45.48.

Found %: Br 38.06; S 15.00. $C_6H_{11}OBrS$. Calculated %: Br 37.94; S 15.16.

Preparation of 2-bromopropyl thiolbutyrate. For reaction we took 8 g of butyryl bromide and 4 g of propylene sulfide. We obtained 8.5 g (71%) of 2-bromopropyl thiolbutyrate.

B. p. 110° (14 mm), d_4^{18} 1.2745, n_D^{18} 1.4920, MR_D 51.05; calc. 50.10.

Found %: Br 35.83; S 14.01. $C_7H_{13}OBrS$. Calculated %: Br 35.6; S 14.22.

Preparation of 2-bromopropyl thiolbenzoate. For reaction we took 10 g of benzoyl bromide and 4 g of propylene sulfide. We obtained 6 g (43%) of 2-bromopropyl thiolbenzoate with b. p. 158° (15 mm) (partial decomposition) and d_4^{20} 1.3850.

Found %: Br 31.17; S 12.14. $C_{10}H_{11}OBrS$. Calculated %: Br 30.9; S 12.36.

Preparation of 2-(acetothio)propyltrimethylammonium iodide. A mixture of 14 g of 2-iodopropyl thiolacetate, obtained by the reaction of acetyl iodide with propylene sulfide, and 25 ml of dry ether was placed in a round-bottomed flask. Three grams of trimethylamine was gradually added to the solution cooled to -10°.

After all of the amine had been added the reaction mixture was allowed to stand in the cold for 5-6 hours and then for another 3 days at room temperature. The obtained precipitate of 2-(acetothio)-propyltrimethylammonium iodide was filtered and then recrystallized three times from butanol. After 3 recrystallizations we obtained 8.6 g (50.6%) of substance with m. p. 234°.

Found %: N 3.4; I 35.5; S 10.2. $C_8H_{18}ONIS$. Calculated %: N 4.6; I 35.3; S 10.5.

A mixture of this compound with acetyl β-methylthiocholine iodide, obtained by the Renshaw method, melted at 131-134°.

SUMMARY

1. Ethylene sulfide and propylene sulfide were reacted with the chlorides of di- and trichloroacetic acids, and with the bromides of acetic, bromoacetic, propionic, butyric and benzoic acids. The corresponding compounds were obtained.

2. The new compounds-chloroethyl trichlorothiolacetate, 2-chloropropyl chlorothiolacetate, 2-chloropropyl dichlorothiolacetate, 2-chloropropyl trichlorothiolacetate, 2-bromoethyl thiolacetate, 2-bromoethyl bromothiolacetate, 2-bromoethyl thiolpropionate, 2-bromoethyl thiolbutyrate, 2-bromoethyl thiolbenzoate, 2-bromopropyl thiolacetate, 2-bromopropyl bromothiolacetate, 2-bromopropyl thiolpropionate, 2-bromopropyl thiolbutyrate, 2-bromopropyl thiolbenzoate and acetyl α-methylthiolcholine iodide were synthesized and described.

3. It was determined that acetyl iodide adds to propylene sulfide with the formation of 2-iodo-n-propyl thiolacetate.

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Received November 23, 1956

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[*] Original Russian pagination. See C. B. Translation.

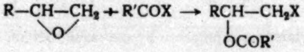
REACTION OF HALIDES OF CARBOXYLIC ACIDS WITH ALIPHATIC α-OXIDES

S. Z. Ivin

Only a few studies, devoted to the reaction of halides of carboxylic acids with aliphatic α-oxides, are known in the literature. Thus, for example, the reaction of acetyl chloride and acetyl iodide with ethylene oxide [1], of acetyl bromide with propylene oxide [2], and of acetyl chloride with epichlorohydrin [3], are described.

We made a more detailed study of the reaction of some bromides and iodides of carboxylic acids with ethylene oxide, propylene oxide and epichlorohydrin.

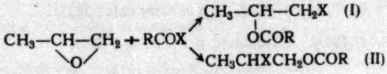
Acid bromides and iodides readily add to alkylene oxides with the formation of the corresponding 2-haloalkyl carboxylic acid esters according to the scheme



$$R{-}\underbrace{CH{-}CH_2}_{O} + R'COX \rightarrow R\underset{OCOR'}{CH}{-}CH_2X$$

The reactions were run in anhydrous carbon tetrachloride medium with ice-water cooling. The addition of the acid halides to alkylene oxides is practically complete by the time all of the α-oxide has been added to the acid halide. The resulting 2-haloalkyl carboxylic esters were obtained as pure compounds, and their yields reached 70-85%.

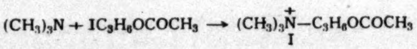
The reaction of propylene oxide with acid halides can proceed in two directions with the formation of either the 2-haloisopropyl carboxylate (I) or the 2-halo-n-propyl carboxylate (II).



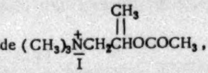
$$CH_3{-}\underbrace{CH{-}CH_2}_{O} + RCOX \begin{array}{l} \nearrow CH_3{-}\underset{OCOR}{CH}{-}CH_2X \quad (I) \\ \searrow CH_3CHXCH_2OCOR \quad (II) \end{array}$$

The direction of this reaction was studied on the example of adding acetyl iodide to propylene oxide. To determine the direction of reaction we used the method of comparing the melting point of the crystalline derivative of the reaction product between propylene oxide and acetyl iodide with the melting point of the corresponding compound of known structure.

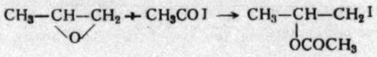
To obtain the crystalline derivative we added the reaction product of propylene oxide with acetyl iodide to trimethylamine in known manner [4].



$$(CH_3)_3N + IC_3H_6OCOCH_3 \rightarrow (CH_3)_3\underset{I}{\overset{+}{N}}{-}C_3H_6OCOCH_3$$

The 2-acetopropyltrimethylammonium iodide obtained in this manner melted at 175° and proved to be identical with 2-methylacetylcholine iodide  $(CH_3)_3\underset{I}{\overset{+}{N}}CH_2\overset{CH_3}{C}HOCOCH_3$, which according to the literature has m. p. 174° [5]. A mixture of these two compounds failed to show a melting point depression.

The identity of the synthesized methylacetylcholine iodide with 2-methylacetylcholine iodide indicates that the reaction product of acetyl iodide with propylene oxide was 2-iodoisopropyl acetate (I). Consequently, the addition of acetyl iodide to propylene oxide proceeds by the first direction



EXPERIMENTAL

Preparation of 2-bromoethyl acetate. A mixture of 20 g of acetyl bromide and 30 ml of dry carbon tetrachloride was placed in a round-bottomed flask fitted with reflux condenser and dropping funnel. Then 7.2 g of ethylene oxide was added in drops with ice-water cooling.

When all of the ethylene oxide had been added the reaction mixture was heated at 40-50° for 20 minutes. The formed 2-bromoethyl acetate was vacuum-distilled. Yield 20 g (74%).

B. p. 160° (750 mm), d_4^{23} 1.502, n_D^{23} 1.457. MR_D 30.20; calc. 30.08.

Found %: C 28.6; H 4.4; Br 48.21. $C_4H_7O_2Br$. Calculated %: C 28.8; H 4.5; Br 48.0.

The other 2-haloalkyl carboxylates were prepared by the same method used to obtain 2-bromoethyl acetate.

Preparation of 2-bromoethyl bromoacetate. For reaction we took 10 g of bromoacetyl bromide, 20 ml of carbon tetrachloride and 2.1 g of ethylene oxide. We obtained 5.2 g (43%) of compound.

B. p. 85° (5 mm), d_4^{16} 1.970 n_D^{16} 1.526, MR_D 38.30; calc. 38.86.

Found %: C 19.31; H 2.3; Br 65.4. $C_4H_6O_2Br_2$. Calculated %: C 19.5; H 2.4; Br 65.0.

Preparation of 2-iodopropyl acetate. For reaction we took 25 g of acetyl iodide, 40 ml of carbon tetrachloride and 8.5 g of propylene oxide. We obtained 20 g (60%) of 2-iodopropyl acetate.

B. p. 64° (7-8 mm), d_4^{14} 1.6762, n_D^{14} 1.4900, MR_D 39.35; calc. 38.93.

Found %: C 26.2; I 55.8. $C_5H_9O_2I$. Calculated %: C 26.2; I 55.6.

Preparation of 2-bromopropyl propionate. For reaction we took 13.7 g of propionyl bromide and 5.8 g of propylene oxide. We isolated 16 g (82%) of compound.

B. p. 68° (12 mm), d_4^{18} 1.3253, n_D^{18} 1.4500, MR_D 39.25; calc. 38.34.

Found %: C 36.6; Br 41.4. $C_6H_{11}O_2Br$. Calculated %: C 36.9; Br 41.05.

Preparation of 2-bromoethyl benzoate. For reaction we took 15 g of benzoyl bromide and 4 g of ethylene oxide. We isolated 7.8 g (41%) of 2-bromoethyl benzoate with b. p. 130° (10 mm).

Found %: C 45.4; Br 35.2. $C_9H_9O_2Br$. Calculated %: C 45.6; Br 35.0.

Preparation of 2-bromoethyl propionate. For reaction we took 7 g of propionyl bromide and 2.2 g of ethylene oxide. We obtained 7.6 g (83%) of compound.

B. p. 67° (10 mm), d_4^{20} 1.3820, n_D^{20} 1.454. MR_D 35.01; calc. 34.71.

Found %: C 33.10; Br 44.30. $C_5H_9O_2Br$. Calculated %: C 33.2; Br 44.15.

Preparation of 2-bromoethyl butyrate. For reaction we took 8 g of butyryl bromide and 2.4 g of ethylene oxide. We isolated 8 g (77%) of 2-bromoethyl butyrate.

B. p. 75° (12 mm), d_4^{19} 1.3258, n_D^{19} 1.4510. MR_D 39.54; calc. 38.34.

Found %: C 36.56; Br 41.35. $C_6H_{11}O_2Br$. Calculated %: C 36.9; Br 41.05.

Preparation of 2-bromopropyl butyrate. For reaction we took 3.5 g of butyryl bromide and 0.8 g of propylene oxide. We obtained 2.6 g (60%) of compound.

B. p. 83° (14 mm), d_4^{20} 1.2568, n_D^{20} 1.438. MR_D 44.28; calc. 42.94.

Found %: C 40.00; Br 38.5. $C_7H_{13}O_2Br$. Calculated %: C 40.1; Br 38.3.

Preparation of 2-bromopropyl benzoate. For reaction we took 5.5 g of benzoyl bromide and 1.8 g of propylene oxide. We obtained 4.5 g (61%) of compound with b. p. 140° (12 mm) and d_4^{20} 1.3504.

Found %: C 49.19; Br 33.21. $C_{10}H_{11}O_2Br$. Calculated %: C 49.35; Br 32.9.

Preparation of 2-bromo-2-chloropropyl bromoacetate. For reaction we took 10 g of bromoacetyl bromide and 5 g of epichlorohydrin. We obtained 9 g (60%) of compound.

B. p. 115° (5 mm), d_4^{16} 1.901, n_D^{16} 1.5270, MR_D 49.10; calc. 48.34.

Found %: C 20.1; Br 54.45; Cl 12.20. $C_5H_7O_2Br_2Cl$. Calculated %: C 20.4; Br 54.36; Cl 11.85.

Preparation of 2-bromo-2-chloropropyl propionate. For reaction we took 7 g of propionyl bromide and 5.2 g of epichlorohydrin. We obtained 8.5 g (69%) of 2-bromo-2-chloropropyl propionate.

B. p. 96° (12 mm), d_4^{20} 1.4500, n_D^{20} 1.4750, MR_D 44.51; calc. 43.10.

Found %: C 31.1; Br 35.2; Cl 15.7. $C_6H_{10}O_2BrCl$. Calculated %: C 31.4; Br 35.00; Cl 15.50.

Preparation of 2-bromo-2-chloropropyl acetate. For reaction we took 10 g of acetyl bromide and 7.5 g of epichlorohydrin. We obtained 14 g (80%) of compound.

B. p. 93° (15 mm), d_4^{25} 1.536, n_D^{25} 1.4818, MR_D 40.00; calc. 39.58.

Found %: C 27.7; Br 37.5; Cl 16.75. $C_5H_8O_2BrCl$. Calculated %: C 27.9; Br 37.2; Cl 16.5.

Preparation of 2-chloro-2-iodopropyl acetate. For reaction we took 10 g of acetyl iodide and 5.4 g of epichlorohydrin. We obtained 12 g (78%) of compound.

B. p. 110° (15 mm), d_4^{16} 1.785, n_D^{16} 1.5240, MR_D 44.70; calc. 43.80.

Found %: C 22.68; I 48.2; Cl 13.75. $C_5H_8O_2ClI$. Calculated %: C 22.90; I 48.4; Cl 13.50.

Preparation of 2-bromo-2-chloropropyl benzoate. For reaction we took 9.3 g of benzoyl bromide and 5.2 g of epichlorohydrin. We obtained 7 g (48%) of 2-bromo-2-chloropropyl benzoate with b. p. 157-162° (10 mm) and d_4^{22} 1.4602.

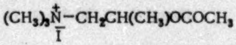
Found %: C 40.41; Br 30.2; Cl 13.65. $C_{10}H_{10}O_2ClBr$. Calculated %: C 40.70; Br 30.00; Cl 13.40.

Preparation of 2-acetopropyltrimethylammonium iodide. Into a round-bottomed flask was placed 9.7 g of 2-iodopropyl acetate, obtained by the addition of acetyl iodide to propylene oxide, and 30 ml of dry ether.

To the solution, cooled to -15°, was gradually added 2.5 g of trimethylamine with shaking. When all of the amine had been added the flask was stoppered and allowed to stand in the cold for 4-6 hours and then for another 3 days at room temperature.

The obtained precipitate of 2-acetopropyltrimethylammonium iodide was filtered and recrystallized twice from butanol. We obtained 8.1 g (66%) of compound with m. p. 175°.

Found %: C 33.10; N 4.31; I 44.5. $C_8H_{18}O_2NI$. Calculated %: C 32.85; N 4.9; I 44.2.

A mixture of the obtained substance with acetyl β-methylcholine iodide  $(CH_3)_3\underset{I^-}{\overset{+}{N}}-CH_2CH(CH_3)OCOCH_3$ melted at 175°, i.e., the m. p. was not depressed.

SUMMARY

1. Ethylene oxide, propylene oxide and epichlorohydrin were reacted with acetyl bromide, bromoacetyl bromide, acetyl iodide, propionyl bromide, butyryl bromide and benzoyl bromide.

2. The compounds 2-iodopropyl acetate, 2-bromopropyl propionate, 2-bromoethyl propionate, 2-bromoethyl butyrate, 2-bromopropyl butyrate, 2-bromopropyl benzoate, 2-bromo-2-chloropropyl bromoacetate, 2-bromo-2-chloropropyl propionate, 2-chloro-2-iodopropyl acetate and 2-chloro-2-bromopropyl benzoate were obtained for the first time and their properties characterized.

3. It was established that acetyl iodide adds to propylene oxide with the formation of 2-iodoisopropyl acetate.

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Received November 23, 1956

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* Original Russian pagination. See C. B. Translation.

SULFONATION REACTION

XLVI. EQUILIBRIUM BETWEEN TOLUENETRISULFONIC ACID AND ITS TRICHLORIDE

A. A. Spryskov and Iu. L. Kuz'mina

It was shown earlier [1] that between sulfonic acids and their chlorides in a medium composed of a mixture of sulfuric and chlorosulfonic acids equilibrium is established according to the equation

$$RSO_2Cl + H_2SO_4 \rightleftarrows RSO_3H + HSO_3Cl$$

It was mentioned [1d] that as a rule the values of the equilibrium constants for the di- and trisulfonic acid derivatives are higher than for the monosulfonic acid derivatives.

Below we describe the results of studying the equilibrium for still another case involving polysulfonic acid derivatives, namely that of 2,4,6-toluenetrisulfonyl chloride with the corresponding trisulfonic acid in a mixture of sulfuric and chlorosulfonic acids. The toluenetrisulfonyl chloride (m. p. 162°), obtained by the earlier described method [2], was added to mixtures of chlorosulfonic and sulfuric acids of variable composition, contained in small ground-glass stoppered flasks. After the trichloride had dissolved the solutions were kept at a temperature of 80 ± 1°, and then the reaction mixtures were poured over ice. The deposited trichloride was filtered, washed, dried, and weighed. The reaction mixtures were kept at 80° for 10 hours, since from a series of experiments it was found that this length of time at 80° is sufficient to reach a condition close to equilibrium.

The chlorosulfonic acid used in the experiments had b. p. 86-88° at 20-25 mm, and contained 2.4% sulfuric acid.

As had already been shown by us earlier [1c], for the case of polysulfonic acid derivatives equilibrium is established between the polysulfonyl chloride and the sulfonyl chloride of the sulfonic acid. The equilibrium constant for the trisulfo derivatives of toluene is calculated starting with the equation

$$CH_3C_6H_2(SO_2Cl)_3 + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_2Cl)_2SO_3H + HSO_3Cl,$$

i.e., the disulfonyl chloride of the sulfonic acid is formed, which can then suffer further transformation to the sulfonyl chloride of the disulfonic acid, and then to the trisulfonic acid by the equations:

$$CH_3C_6H_2(SO_2Cl)_2SO_3H + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_2Cl)(SO_3H)_2 + HSO_3Cl,$$
$$CH_3C_6H_2(SO_2Cl)(SO_3H)_2 + H_2SO_4 \rightleftarrows CH_3C_6H_2(SO_3H)_3 + HSO_3Cl$$

The transformations according to the last two equations either proceed at a much slower rate than does the transformation according to the first equation, or else the equilibrium constants of the last two reactions are exceedingly small.

If for 1 mole of the trisulfonyl chloride we take m moles of sulfuric acid and n moles of chlorosulfonic acid, then the equilibrium constant based on the first equation is determined by the formula

$$k = \frac{[x][n+x]}{[1-x][m-x]},$$

where x corresponds to the number of moles of the trisulfonyl chloride converted to the disulfonyl chloride of the sulfonic acid.

The experimental results given in Table 1, permit determining the equilibrium constant, and from this it becomes possible to calculate the values of x using the formula

$$x = \frac{n+k+km \pm \sqrt{(n+k+km)^2 - 4(k-1)km}}{2(k-1)}$$

The computed values of x are given in the last column of Table 1, and as can be seen, differ from the experimentally found values (Column 4, Table 1) by approximately 1-2%.

TABLE 1

Equilibrium Between 2,4,6-Toluenetrisulfonic Acid and Its Trichloride at 80 ± 1°

Expt. Nos.	Moles /1 mole chloride		Chloride isolated (%)	Equilibrium constant k	Cl computed by the formula (%)
	H_2SO_4	HSO_3Cl			
212	1.04	9.51	83.7	2.15	82.0
219	1.32	9.53	79.7	2.23	78.0
216	3.86	13.32	60.3	2.61	61.3
217	3.42	12.46	60.2	2.81	62.5
215	4.32	12.34	55.5	2.64	56.7
213	4.31	10.23	51.9	2.59	51.3
			Average	2.50	

DISCUSSION OF RESULTS

We studied a total of 8 cases of equilibrium between sulfonic acids and their chlorides starting with the chloride which, in a mixture of sulfuric and chlorosulfonic acids, is converted to the sulfonic acid up to equilibrium. In practice it is usually necessary to convert the sulfonic acids or their sodium salts to the chlorides. The sulfonic acids are converted directly to the chlorides in the sulfonation mass obtained by adding the sulfonic acid in question to chlorosulfonic acid. The sodium sulfonates are converted to the chlorides by adding the dry salt to chlorosulfonic acid.

The found equilibrium constants reveal that sulfonic acids behave quite differently in their conversion to chlorides. Thus, polysulfonic acids, possessing as a rule higher equilibrium constants, are converted to the chlorides in smaller yields than are the monosulfonic acids.

In Table 2 we give the results of calculating the yield of chloride, starting with the sulfonic acid, when 5 moles of chlorosulfonic acid are taken per sulfonic group, and also the amount of chlorosulfonic acid required to give the chloride in 90% yield. In all previously described experiments we started with the chloride, sulfuric acid and chlorosulfonic acid. In order to be able to utilize all of the earlier used formulas, we conditionally brought all of the substances to the same original state. Thus, 1 mole of sulfonic acid with 5 moles of chlorosulfonic acid is conditionally converted completely to 1 mole of the chloride and 1 mole of sulfuric acid, while 4 moles of chlorosulfonic acid remain. This mixture is now reacted to the equilibrium state. The given data reveal that to obtain a high yield of polysulfonyl chloride it is frequently necessary to take very large amounts of chlorosulfonic acid.

We also compared the yields of chloride obtained when the sulfonic acid and its sodium salt were reacted with chlorosulfonic acid. The reaction of 1 mole of sodium 2,5-dichlorosulfonate with 5 moles of chlorosulfonic acid and 0.005 mole of sulfuric acid gives the chloride in 79% of the theoretically possible yield, as is shown by calculation using the method published in the paper devoted to a study of the equilibrium between the sodium sulfonate or the sulfonic acid and the chloride [3]. The yield of chloride from the free sulfonic acid under the same conditions reaches 87.8%. Consequently, to obtain the same yields of chloride from sodium sulfonates requires larger amounts of chlorosulfonic acid than when the corresponding free sulfonic acids are used.

TABLE 2

Conversion of Sulfonic Acids to Their Chlorides

Acid	k	Using 5 moles HSO_3Cl/sulfonic group (%)	HSO_3Cl required/sulfonic group to give 90% Cl yield (moles)
m-Nitrobenzenesulfonic acid	0.51	90.0	5.0
2,5-Dichlorobenzenesulfonic acid	0.64	88.9	6.1
p-Toluenesulfonic acid	1.18	81.4	10.5
m-Sulfobenzoic acid	1.22	81.0	10.8
2,4-Toluenedisulfonic acid	0.90	83.0	17.3
1,3-Benzenedisulfonic acid	1.33	77.7	24.6
1,3,5-Naphthalenetrisulfonic acid	1.90	70.5	52.5
2,4,6-Toluenetrisulfonic acid	2.50	65.3	68.2

However, in practice high yields of the chlorides are obtained even when a much smaller excess of chlorosulfonic acid than that indicated above is used. This happens in the cases where the formed chloride precipitates from solution, as a result of which the equilibrium is shifted in the direction of forming more chloride.

SUMMARY

The equilibrium between 2,4,6-toluene trisulfonic acid and its trichloride was studied in a medium composed of chlorosulfonic and sulfuric acids, at 80°. The equilibrium constant was found to be 2.50.

It was shown that to obtain equal yields of the chlorides, starting with polysulfonic acids, requires larger amounts of chlorosulfonic acid per sulfonic group than when starting with monosulfonic acids. To obtain an equal yield of the chloride from the sodium sulfonates requires larger amounts of chlorosulfonic acid than when the corresponding free sulfonic acids are used.

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Received December 17, 1956

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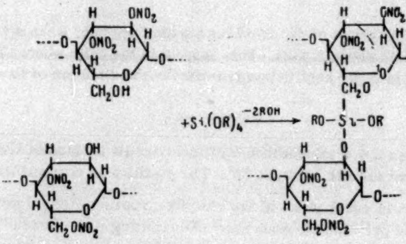
*Original Russian pagination. See C. B. Translation.

REACTION OF SOME ORGANOSILICON COMPOUNDS WITH CELLULOSE NITRATES

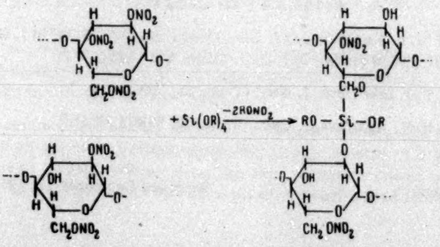
A. P. Kreshkov, I. Ia. Guretskii and P. A. Andreev

We had shown [1-6] that alkoxy- and alkoxyhalosilanes, alkyl and arylalkoxysilanes, alkyl-arylhalosilanes and the products of their hydrolytic cleavage and subsequent condensation, and also many other mono-, di-, tri- and tetrafunctional organosilicon compounds show double decomposition reaction with various inorganic and organic compounds, containing in their molecule either active atoms or functional groups (H, Cl, OH, OR, NH$_2$, etc.). The products obtained in this manner prossess valuable properties [7-10]. Such products, for example, are the high-molecular compounds based on organosilicon compounds and cellulose nitrate, obtained for the first time in the D. I. Mendeleev Moscow Chemical Technological Institute [11], which compounds possess high hydrophobicity, high heat and acid resistance, and good electrical insulation properties [12-15]. However, the processes for the reaction of organosilicon compounds with cellulose nitrates have remained unstudied right up to now.

The present paper is devoted to a study of the indicated reaction. Our investigations revealed that depending on the conditions the following processes are observed. 1) Exchange reaction of the starting organosilicon compounds with the free hydroxyl groups of the cellulose nitrate, accompanied by the joining together of the nitrocellulose macromolecule and the silicon atoms through the oxygen



2) Transesterification of the nitrate ester



The formation of more complex coupling products of organosilicon compounds with cellulose nitrates is possible, observed when the reaction is run in the presence of hydrogen chloride.

EXPERIMENTAL

The starting cellulose nitrate was pyroxylin containing 11.89% nitrogen, 0.50% moisture and 0.3% ash. As the starting organosilicon compounds we used various tetraalkoxysilanes and alkylalkoxysilanes, synthesized and purified by methods described in the literature [15]. The physical constants of all of the starting compounds agreed with the literature data.

It had been established by us [11] that the heating of cellulose nitrate solutions in a mixed solvent (for example, in a mixture of acetone, ethyl acetate and methyl alcohol, taken in the mole ratio 1 : 0.2 : 2.5) with tetraalkoxysilanes and alkylalkoxysilanes, and also with the products of their chemical transformations, leads to the formation of siliconitrocellulose compounds. The method given below was used by us to isolate and study the individual fractions of the compounds obtained in this manner. A mixture of 50 g of the starting pyroxylin and 450 g of acetone was placed in a three-necked flask, fitted with an oil-seal mechanical stirrer and thermometer. The mixture was stirred until a homogeneous acetone solution of cellulose nitrate was obtained. Then the obtained solution was maintained with constant stirring on the water bath at 55-57° for 3-18° hours. After this the flask contents were cooled and decanted into a beaker containing benzene. The obtained mixture was allowed to stand for 15 hours. Here a precipitate of cellulose nitrate deposited. The isolated precipate was pressed, broken up, and dried in a steam chest for 6 hours at 95-97°. The dried cellulose nitrate was subjected to elemental analysis.

Found %: N 11.31; C 28.40; H 3.40. $C_6H_7O_2(ONO_2)_{2.06}(OH)_{0.94}$. Calculated %: N 11.32; C 28.24; H 3.12.

Using similar conditions, a solution of pyroxylin, heated to 55°, was treated with various esters of orthosilicic acid in an amount oorresponding to a mole ratio of $C_6H_7O_2(ONO_2)_2OH : Si(OR)_4$ equal to 1 : 1. The time of heating ranged from 5 to 15 hours. The analysis data for the obtained products reveal that the amount of silicon in the product increases gradually the longer the acetone solution of cellulose nitrate is heated with the tetraethoxysilane. The amount of silicon in the obtained products reaches 0.3-0.55%, and the nitrogen content 11.32-11.25%.

In order to remove the organosilicon compounds the obtained products were reprecipitated three times and then washed with benzene. The analysis data for the washed products, and for those obtained from the mother liquor, revealed that both had practically the same silicon and nitrogen content.

By means of special experiments with tetraethoxysilane it was observed that even traces of chlorosilanes exert a sharp influence on the reaction of tetraethoxysilane with cellulose nitrate. The elementary composition of the reaction products obtained under these conditions differed sharply from the elementary composition of the products synthesized from chemically pure compounds.

In order to study the reaction of other esters of orthosilicic acid with cellulose nitrates, and also to study the influence of chloroderivatives of silane on the process, we ran a series of experiments with chemically

TABLE 1

Elementary Composition of Reaction Products of Cellulose Nitrate with Alkoxysilanes, Containing $SiCl_4$

Formula of alkoxysilane	Elementary composition (%)			
	N	Si	C	H
$(CH_3O)_4Si$	9.76	7.65	28.52	3.32
$(C_2H_5O)_4Si$	10.64	3.75	29.18	3.13
n -$C_4H_9O)_4$ Si . . .	10.66	1.53	30.48	3.67
iso -$C_5H_{11}O)_4Si$ . . .	9.86	0.76	32.70	4.49

pure tetramethoxy-, tetraethoxy-, tetra-n-butoxy- and tetraisoamyloxysilanes, and with the same esters containing chloroderivatives. The reaction conditions were similar to those described above. The compounds, obtained by the reaction of chemically pure alkoxysilanes with cellulose nitrate, had a silicon content of the order of 0.15-0.7%. The elemental analysis data for the reaction products of cellulose nitrate with the indicated alkoxysilanes, containing 0.01% $SiCl_4$, are given in Table 1.

With increase in the amount of chloroderivatives in the alkoxysilanes the amount of nitrogen decreases, and the amount of silicon increases. The presence of large amounts of chloroderivatives in the starting alkoxysilanes leads to the formation of a solid insoluble compound, whereas the reaction products of the chemically pure alkoxysilanes with cellulose nitrates are soluble. Using similar conditions, we ran some experiments with a cellulose nitrate containing 12.39% nitrogen. Full compliance with the above described rules was also observed in this series of experiments.

We also ran some experiments with alkylalkoxysilanes that contained chlorosilanes. The analysis data for the obtained products are given in Table 2.

TABLE 2

Amount of Nitrogen and Silicon in Reaction Products of Cellulose Nitrate (11.87% N) with Alkylalkoxysilanes, Containing 0.01% $SiCl_4$

Formula of alkylalkoxysilane	N (%)	Si (%)
$(CH_3)_3Si(OCH_3)$	10.64	0.26
$(C_2H_5)_2Si(OCH_3)_2$	10.07	1.23
$(C_2H_5)_2Si(OC_2H_5)_2$	10.10	1.58

We also ran a series of experiments in which the various cellulose nitrates were heated with alkoxysilanes in the absence of a solvent. In the experiments with tetramethoxysilane the heating was at 110-120°, and in the experiments with tetraethoxysilane it was at 130-155°. The cellulose nitrate and orthosilicic ester were taken in such amount that all of the cellulose nitrate was found dissolved in the alkoxysilane. In all of the experiments the cellulose nitrate showed swelling clear up to gelatinization. The reaction products were pressed, repeatedly washed with benzene, and dried. In this series of experiments the evolution of the corresponding alcohol and of nitrogen oxides was observed, which can serve as evidence that the alkoxysilanes react with both the hydroxyl groups and the nitrate groups of cellulose nitrate. The elemental analysis data for the obtained products are given in Table 3.

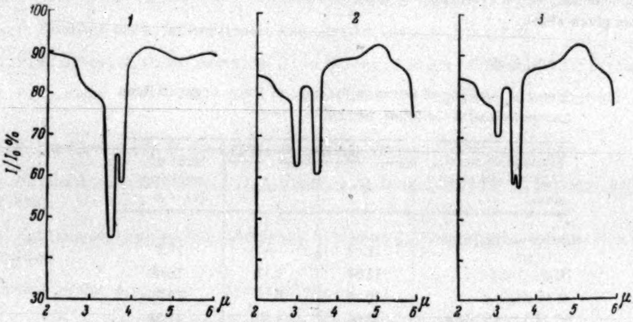
TABLE 3

Elementary Composition of Reaction Products of Alkoxysilanes with Cellulose Nitrate in Heterogeneous Medium

Formula of starting alkoxysilane	N in cellulose nitrate (%)	Elementary composition (%)			
		N	Si	C	H
$(CH_3O)_4Si$	11.89 12.39 13.36	10.03 10.54 10.80	3.24 3.74 6.56	29.43 28.04 28.12	3.72 3.31 3.23
$(C_2H_5O)_4Si$	11.89 12.39 13.36	9.26 9.80 11.20	1.52 2.83 1.59	30.72 32.17 29.68	3.70 3.56 3.21

The reaction of cellulose nitrate with alkoxysilanes, containing chloro derivatives, gave products with a nitrogen content of 7 to 11%, and a silicon content of 3 to 10%.

We also studied the infrared spectra of the reaction products of tetraethoxysilane with cellulose nitrate (11.87% N) The starting product contained 0.55% silicon. The investigation was run using an IKS-11 spectrometer and NaCl prism. The cellulose nitrate and its reaction product with tetraethoxysilane were studied as films, having a thickness of 19-20 μ, obtained from solutions of these products in acetone by evaporation of the solvent in vacuo. The spectrum of $(C_2H_5O)_4Si$ was taken as a 20% solution in CCl_4 in the interval of 2-6μ using a NaCl cuvette and a layer thickness of 0.1 mm. The absorption curves of cellulose nitrate, of tetraethoxysilane, and of their reaction product, are shown in the Figure. The absorption at 2.8-3 and at 3.5 μ is respectively due to the vibrations of the OH and CH groups [16-20]. In the given wavelength intervals, as well as throughout the whole spectrum, the absorption curve for the reaction product of tetraethoxysilane with cellulose nitrate shows all of the main characteristic absorption maxima, belonging to both cellulose nitrate and to tetraethoxysilane. A substantial reduction in the absorption maximum is observed at 3 μ. This permits the conclusion that the reaction of tetraethoxysilane with cellulose nitrate under the above indicated conditions proceeds with a reduction in the number of hydroxyl groups.



Infrared absorption curves. 1) Tetraethoxysilane, 2) cellulose nitrate, 3) cellulose nitrate, reacted with tetraethoxysilane.

After precipitating the product from acetone solution with benzene, the acetone-benzene mixture, obtained as a clear liquid, was fractionally distilled. The distillate, obtained from the first distillation, was fractionated through a column with an efficiency of 25 theoretical plates. The head fraction was shown to contain alcohols, corresponding to the starting alkoxysilane [20].

Using the method of ultraviolet spectroscopy, it was shown that, together with nitrogen oxides, an alkyl nitrate was present in the reaction products. This indicates that the nitrate groups of nitrocellulose react with the alkoxy groups of organosilicon compounds. Such a reaction course is in agreement with the studies of S. N. Danilov, who showed that under certain conditions the reaction of cellulose nitrate with acetic acid leads to replacement of the nitrate groups by the acetyl group [23].

We also determined the heats of swelling of the obtained products in acetone [21, 22] (cf. Table 4).

From the data of Table 4 it can be seen that the heats of swelling of the obtained compounds decrease with increase in the amount of silicon in them.

The solubility of the reaction products in various polar and nonpolar solvents, and in their mixtures, was studied. It was found that the solubility of the obtained products decreases with increase in the amount of silicon in them. The products containing up to 1% silicon are readily soluble in pyridine, acetone, alcohol-ether mixtures, cyclohexanone, alkyl acetates, in mixtures of the latter with toluene and xylene, in nitrobenzene, and in camphor. Increasing the silicon content above 1% leads to a loss in the solubility of the products in the indicated solvents.

As a result, based on the obtained data it can be assumed that the indicated organosilicon compounds, react with the hydroxyl groups, and under certain conditions, also with the nitrate groups of cellulose nitrate, as is evidenced by the evolution of an alcohol and nitrogen oxides.

The presence of chlorosilane impurities in the alkoxy- and alkylalkoxysilanes hastens this process considerably, as can be judged by the amount of silicon in the obtained products.

It is known that the dissolving of cellulose nitrates is accompanied by the formation of chemical adducts between the functional groups of the cellulose nitrate and the solvent [24-26] and this process can be characterized by the heat effect of solution. A decrease in the heat of swelling with increase in the amount of silicon in the products obtained by us points to a reduction in the amount of active functional groups in the cellulose nitrate. Analysis of the obtained products by the method of infrared spectroscopy also indicates this. The solubility of cellulose nitrates to a considerable degree characterizes their structure. A reduction in the solubility of the products obtained by us with increase in their silicon content can be explained by the formation of chemical bonds in the reaction of the functional groups of cellulose nitrates with the alkoxy groups of organosilicon compounds, with the formation of compounds having a tridimensional structure in accordance with the schemes given above.

TABLE 4

Heats of Swelling of Reaction Products of Some Organosilicon Compounds with Cellulose Nitrate

Formula of starting organosilicon compound	Amount in product (%)		Heat of swelling (cal/g)
	N	Si	
Untreated cellulose nitrate . .	11.89	—	19.2
$(C_2H_5O)_4Si$	11.57	0.17	18.80
n-$(C_4H_9O)_4Si$ . . .	10.60	0.19	19.05
$(C_2H_5)_2Si(OC_2H_5)_2$.	10.05	1.50	15.88
$(C_2H_5O)_4Si$	10.48	4.75	15.01
$(CH_3O)_4Si$	8.50	5.65	14.90

SUMMARY

1. The reaction of tetramethoxy-, tetraethoxy-, tetra-n-butoxy-, tetraisoamyloxy-, trimethylmethoxy-, diethyldimethoxy- and diethyldiethoxysilanes with cellulose nitrates was studied.

2. The infrared spectra and heats of swelling of the reaction products of organosilicon compounds with cellulose nitrates were studied.

3. It was found that during the indicated reaction there occurs a reduction in the number of hydroxyl groups found in the elementary unit of the cellulose nitrate molecule, and also the liberation of an alcohol, both testifying to the fact that the reaction of alkoxysilanes and alkylalkoxysilanes with cellulose nitrates proceeds mainly as the result of reaction with the unesterified hydroxyl groups.

4. It was shown that under certain conditions a reduction in the amount of nitrogen in the reaction products is observed when compared to the starting cellulose nitrate, and also the evolution of nitrogen oxides during reaction, both testifying to the fact that the indicated reaction apparently also proceeds due to transesterification of the nitrate groups of the cellulose nitrate.

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Moscow Chemical Technological Institute

Received November 27, 1956

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*In Russian.

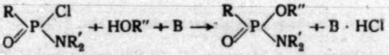
**Original Russian pagination. See C. B. Translation.

DERIVATIVES OF ALKYLPHOSPHONOUS AND PHOSPHONIC ACIDS

[redacted] VIII. SYNTHESIS AND PROPERTIES OF SOME ALKYLATED AMIDES OF ALKYLPHOSPHONIC CHLORIDES

A. I. Razumov, O. A. Mukhacheva and E. A. Markovich

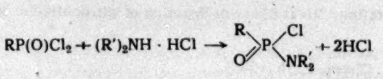
We studied several different routes for the synthesis of biologically active amide esters of alkylphosphonic acids. As it proved later, the best method was found to be the ammonolysis of the chlorides of alkylalkoxyphosphonic acids [1, 2]. However, in addition to the indicated method, we also studied the alkoxylation of the amides of alkoxyphosphonic chlorides with alcohols in the presence of either bases or alcoholates.



$$\mathrm{R(O{=})P(Cl)(NR'_2)} + \mathrm{HOR''} + \mathrm{B} \longrightarrow \mathrm{R(O{=})P(OR'')(NR'_2)} + \mathrm{B \cdot HCl}$$

It was necessary to obtain the starting alkylated amides of the alkylphosphonic chlorides for the indicated syntheses. Similar compounds with mixed functions were studied quite extensively by Michaelis [3] for the case of phosphoric acid derivatives. These compounds were studied intensively both later and at the present time [4-8]. In recent years the attention of investigators has also been attracted to the corresponding fluoro derivatives [9-11]. Only a very small number of similar alkylphosphonic acid derivatives are known at the present time [12-13].

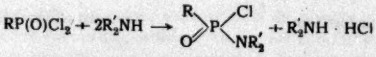
Two methods for the preparation of the alkylated amides of alkylphosphonic chlorides were studied. The first method consisted of the ammonolysis of the full chlorides of the acids with amine hydrochlorides of the Michaelis reaction, known for phosphoric acid derivatives [3].



$$\mathrm{RP(O)Cl_2} + \mathrm{(R')_2NH \cdot HCl} \longrightarrow \mathrm{R(O{=})P(Cl)(NR'_2)} + \mathrm{2HCl}$$

This method gives yields of the order of 30-35% and requires the use of at least 3 times the theoretical amount of the chloride, which for the most part is not recovered.

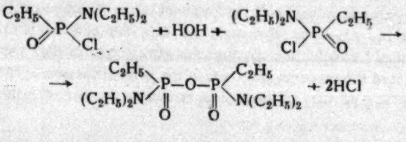
For this reason we gave preference to the method of partial ammonolysis of the full chlorides of primary phosphonic acids.



$$\mathrm{RP(O)Cl_2} + \mathrm{2R'_2NH} \longrightarrow \mathrm{R(O{=})P(Cl)(NR'_2)} + \mathrm{R'_2NH \cdot HCl}$$

Using this method we obtained several members of this series of compounds (Table 1). The ammonolysis with primary amines gives products that cannot be vacuum-distilled; for this reason they were not isolated in a pure state.

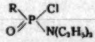
This first member of the amides (Table 1) is a crystalline substance (m. p. 42-43°) that can be vacuum-distilled with ease. The remaining members are liquids with a piercing mint or peppery odor. They fume in the air and are hydrolyzed with exceeding ease by atmospheric moisture. When reacted with water they cleave hydrogen chloride, while the phosphorus-containing radicals combine in pairs.



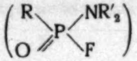
The yield of the obtained alkylpyrophosphonic amides is very small due to further reaction of the formed products with hydrogen chloride, which leads to cleavage of the amide groups and the formation of amine hydrochlorides due to the instability of the P–N bond in an acid medium. If sodium bicarbonate is added to the reaction mixture to bind the formed hydrogen chloride, then the yield of alkylpyrophosphonic acid derivatives rises to 50% and higher.

TABLE 1

Diethylamides of Alkylphosphonic Chlorides



R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for Cl (%)		Analysis for P (%)		Yield (%)
				found	calc.	found	calc.	
CH_3	115–115.5° (9)	1.1274	1.4648	21.16	20.94	—	—	50
C_2H_5	101.5 (3.5)	1.0964	1.4643	—	—	16.59	16.89	65
n.-C_3H_7	112–113 (4)	1.0706	1.4642	—	—	15.43, 15.80	15.69	45
iso-C_3H_7	90–91 (1)	1.0707	1.4627	17.90	17.87	—	—	40
n.-C_4H_9	113–115 (3)	1.0526	1.4641	—	—	14.60, 14.90	14.65	50

The instability of the P–N bond is also manifested in the fluorination of the amides with sodium bifluoride, where the full alkylphosphonic fluorides $RP(O)F_2$ are formed simultaneously with the amides of the alkylphosphonic fluorides  due to rupture of the P–N bond. Consequently, in fluorination we isolated products of both the first and second type (Tables 2 and 3).

The alkylated amides of the alkylphosphonic fluorides are liquids with a faint aromatic odor. They are comparatively resistant to hydrolysis and possess a relatively high toxicity. The full alkylphosphonic fluorides are liquids with an astonishingly tenacious camphor-iodoform odor.

EXPERIMENTAL*

Preparation of Alkylated Amides of Alkylphosphonic Chlorides.

1. Ammonolysis of full alkylphosphonic chlorides with amine hydrochlorides. A mixture of 14 g of diethylamine hydrochloride and 60 g of ethylphosphonic chloride was heated in a flask with reflux condenser

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* The experimental work was done in 1946-1947.

for 6 hours at 235°. The hydrogen chloride was absorbed in a Woulfe bottle containing water. The liquid assumed a brown color. The obtained product was vacuum-distilled. The yield was 7.5 g (35%). The other homologs were obtained in a similar manner.

2. Ammonolysis of full alkylphosphonic chlorides with free amines. The chloride, dissolved in approximately 6 volumes of dry ether, was placed in a flask fitted with reflux condenser, stirrer and dropping funnel. The amine, dissolved in an equal volume of ether, was added at -5°. After all of the amine had been added the reaction product was heated at solvent boil for 30-50 minutes. The hydrochloride was filtered, while the product was vacuum-distilled. All of the other homologs were obtained in a similar manner. It should be mentioned that the amount of hydrochloride obtained was always greater than the theoretical due to atmospheric moisture, which caused the reactions discussed in the general section of this paper. The amides of the phosphonic chlorides with a primary amine radical cannot be vacuum-distilled, for which reason they were used without distilling.

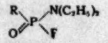
To run the ammonolysis we prepared the full alkylphosphonic chlorides (Table 4) by reacting phosphonic esters with phosphorus trichloride and chlorine. For this we usually took the butyl esters of various phosphonic acids. This method gives good yields.

Synthesis of Diethylpyrophosphonic Bis(Diethylamide).

1. Reaction of water with ethylphosphonic chloride diethylamide. The calculated amount of water was added with vigorous stirring in a rapid nitrogen stream to 46 g of the diethylamide at -10°. The product was quickly vacuum-distilled. The formation of a substantial amount of crystalline product was observed, which proved to be diethylamine hydrochloride (m. p. 217-219°). The yield of main product was 9%.

TABLE 2

Diethylamides of Alkylphosphonic Fluorides



R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for P (%)		Yield (%)
				found	calc.	
CH_3	101° (19)	1.0735	1.4195	20.14, 20.20	20.26	33
C_2H_5	103 (15)	1.0036	1.4130	18.85	18.56	38
n-C_3H_7	110.5 (12)	1.0301	1.4238	17.45, 17.50	17.13	25
iso-C_3H_7	82 (17)	1.0263	1.4231	17.00, 16.85	17.13	34
n-C_4H_9	128—130 (16)	1.0380	1.4358	16.12, 16.29	15.89	30

2. Reaction of sodium bicarbonate with ethylphosphonic chloride diethylamide. For reaction we took 46 g of the amide and 21.5 g of sodium bicarbonate. The synthesis was run in nearly the same manner as described above. After removal of the sodium chloride the product was vacuum-distilled. The hydrochloride was also formed here, but only in small amount (0.2 g). The amount of main product obtained was 20 g (50%).

TABLE 3

Full Alkylphosphonic Fluorides $RP(O)F_2$

R	B. p. (pressure in mm)	d_4^{20}	n_D^{20}	Analysis for P (%)		Yield (%)
				found	calc.	
CH_3	22° (27)	1.3838	1.3277	31.08, 31.15	31.00	10
C_2H_5	44—45 (25)	1.2510	1.3410	26.7	27.10	25
n-C_3H_7	30.5 (13)	1.1791	1.3541	23.96, 23.92	24.21	34
iso-C_3H_7	25 (17.5)	1.1736	1.3512	23.98, 23.91	24.21	10
n-C_4H_9	51.5–52 (17.5)	1.1342	1.3709	21.63, 21.87	21.80	33

B. p. 163.5° – 164.5° at 2 mm, d_4^{20} 1.0619, n_D^{20} 1.4607, MR_D 80.68; calc. 80.57.

Found %: P 20.09; N 8.97, 9.00. $C_{12}H_{30}O_3N_2P_2$. Calculated %: P 19.87; N 8.97.

TABLE 4

Full Alkylphosphonic Chlorides $RP(O)Cl_2$

R	B. p. (pressure in mm)	Yield (%)
CH_3	59—59.5° (11.5)	90
C_2H_5	133.5—134.5 (15)	75
n-C_3H_7	141 (12.5)	75
iso-C_3H_7	113—114 (3)	70
n-C_4H_9	96—98 (15—16)	75

Fluorination of amides of phosphonic chlorides. The proper amide was charged into a Claisen flask, set up for distillation, and then the calculated amount of sodium bifluoride was added. The flask contents were heated to a definite temperature. On conclusion of reaction the product was distilled from the apparatus under a slight vacuum. The heating temperature for the methylphosphonic acid derivative was 110°, for the ethylphosphonic—135°, for the propylphosphonic—150°, and for the butylphosphonic—175°. The obtained mono- and difluoro derivatives were fractionally distilled. An attempt to use sodium fluoride for the fluorination with heating to 180° proved unsuccessful; the product taken for reaction was recovered unchanged.

SUMMARY

1. Some members of the alkylphosphonic acids with mixed functions were synthesized; the alkylated amides of phosphonic chlorides and fluorides, and also the full alkylphosphonic fluorides.

2. It was shown that the alkylated amides of phosphonic chlorides hydrolyze with ease and also that the P—N bond in the alkylated amides of phosphonic fluorides is unstable.

3. The ease with which the alkylated amides of phosphonic chlorides are hydrolyzed by moisture leads to the easy formation of the alkylated amides of alkylpyrophosphonic acids, while the instability of the P—N bond in the amides of phosphonic fluorides leads to the formation of the full fluorides when the indicated amide fluorides are heated.

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Received November 22, 1956

* Original Russian pagination. See C. B. Translation.

SOME ARYL DERIVATIVES OF CYANOTHIOUREA

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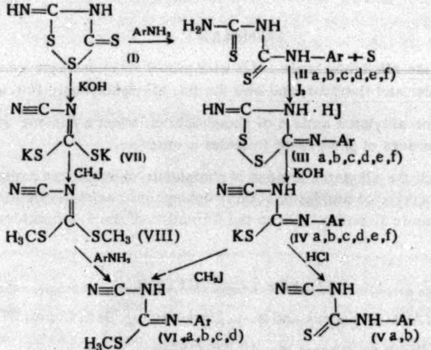
A number of thiourea compounds with biological activity are described in the literature [1]. For the most part recent studies have been devoted to derivatives of aminothiourea (thiosemicarbazide), among which were found compounds with antitubercular activity [2]. Other thiourea derivatives could also be of considerable interest, for example, those containing the physiologically active cyano group. In connection with this we decided to synthesize several N-aryl-N'-cyanothioureas (Ar−NH−CS−NH−C≡N).*



Value of Ar:
a − C_6H_5, b − C_6H_4Cl-p, c − $C_6H_4OCH_3$-p, d − $C_6H_4OCH_3$-o
e − $C_6H_4CH_3$-p f − $C_6H_4CH_3$-o.

The starting substance for the synthesis of the indicated compounds was the readily available 5-imino-3-thio-1,2,4-dithiazolidine (isoperthiocyanic acid, "xanthane hydride") (I). This substance, obtained as early as 1821 by Wohler [3], is formed by the reaction of potassium thiocyanate with sulfuric acid in the cold. When 5-imino-3-thio-1,2,4-dithiazolidine is reacted with aromatic amines the heterocycle is cleaved with the elimination of elemental sulfur and 1-aryldithiobiurets are formed [4]. The dithiobiuret is easily oxidized, again suffering closure into a dithiazolidine compound (III) "thiuret" [5], which in turn when treated with potassium hydroxide is cleaved with the formation of the N-aryl-N'-cyanothiourea as the potassium salt having the iso form (IV).

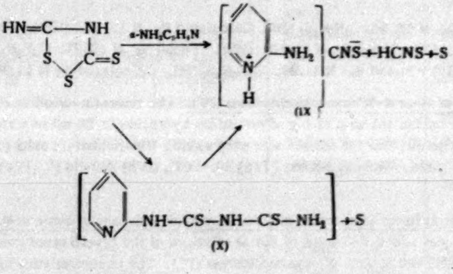
We obtained the potassium salts of the following compounds: N-phenyl- (IVa) [6], p-chlorophenyl- (IVb) [7], p-anisyl (IVc), o-anisyl- (IVd), p-tolyl- (IVe) and o-tolyl-isocyanothiourea (IVf). These salts when reacted with methyl iodide give readily crystallizing methyl esters (VI). These same esters can also be obtained by a shorter method from "xanthane hydride" (I): the reaction of potassium hydroxide with xanthane hydride gives the dipotassium salt of cyanamidodithiocarbonic acid (VII) in 85% yield [8], which when reacted with

* These compounds, having the cyano radical linked to the amino group, can also be regarded as being derivatives of cyanamide.

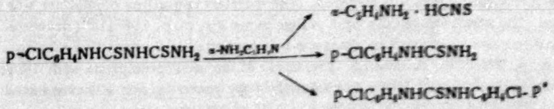
methyl iodide yields the dimethyl ester (VIII) [9]. When the latter is heated with arylamines the methyl esters (VI) are formed in good yields, in particular the p-anisidine compound (VIc), which is identical with the methylation product of the potassium salt of N-(p-anisyl)-N'-cyanoisothiourea.

The free cyanothioureas (V) could be of especial interest. They were isolated by the acidification of the corresponding isothiourea potassium salts (IV) with either hydrochloric or acetic acid. However, these compounds could not be obtained in the pure state, since they are easily changed even when heated in various solvents and migrate into compounds of unknown structure. The free N-phenyl-N'-cyanothiourea (Va) [10] and N-(p-chlorophenyl)-N'-cyanothiourea (Vb) [11] are mentioned in the literature. The N-(p-chlorophenyl)-N'-cyanothiourea (Vb) obtained by us has an ill-defined m. p. of 108-112° (decompn.) which is lower than that indicated in the literature [11]. To identify compound (Vb) we converted it to the potassium salt and then methylated with methyl iodide to give the ester, which proved to be identical with the methyl ester obtained from potassium salt (IVb). This suggests that in our case we were actually dealing with the free N-(p-chlorophenyl)-N'-cyanothiourea, and that the compound described in the literature [11], obtained by a different method, evidently represents a substance of different structure.

An attempt was made by us to obtain cyanothioureas (or the salts of their iso forms), containing instead of aryl either the heterocyclic pyridine or pyrimidine radical. In this connection we postulated that compounds of this nature could be of considerable interest for biological testing. However when α-aminopyridine, and also α-aminopyrimidine, was heated with "xanthane hydride," instead of the desired dithiobiurets we obtained the thiocyanic acid salts of α-aminopyridine (IX) and α-aminopyrimidine, respectively. The formation in these cases of thiocyanic acid salts instead of the α-pyridyl or α-pyrimidinyldithiobiuret can be explained either by the fact that "xanthane hydride" under the influence of either α-aminopyridine or α-aminopyrimidine is decomposed into 2 molecules of thiocyanic acid and sulfur, or by the fact that during the course of reaction the formed dithiobiuret of the heterocycle (X) is unstable and suffers decomposition under the influence of the α-aminoheterocycle.*



Such a reaction course is probably due to the ability of these heterocyclic amines to tautomerize. This postulation finds some support in the fact that even the stable p-chlorophenyldithiobiuret when heated with α-aminopyridine suffers cleavage with the formation of the thiocyanic acid salt of α-aminopyridine; at the same time some p-chlorophenylthiourea and N,N'-bis(p-chlorophenyl)thiourea are also formed.



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* Soon after the conclusion of our work a paper [12] appeared in which a similar case of forming the thiocyanate of α-aminopyridine is mentioned. The mechanism of the reaction is not discussed in the paper.

Apparently, the basicity of the amine is not a decisive factor in this reaction, since when the reaction is run with ammonia, and also with isopropylamine, the p-chlorophenyldithiobiuret fails to suffer any changes.

In water solutions the potassium salts of arylcyanoisothioureas, and also the dipotassium salts of cyanamidodithiocarbonic acid, form precipitates with certain metal salts (cf. EXPERIMENTAL), which are either salts or possibly complex compounds. In connection with this the potassium salts could be of interest for physiological testing and also in analytical chemistry.

When tested in vitro the potassium salts of the cyanoisothioureas, and also the corresponding intermediate products, the dithiobiurets (II), showed only slight activity toward the virulent strain of tubercle bacillus (human type). *

EXPERIMENTAL

5-Imino-3-thio-1,2,4-dithiazolidine ("xanthane hydride") (I) was obtained by the described method [13] using potassium thiocyanate and sulfuric acid. The yield was 20-25% on the weight of potassium thiocyanate.

The aryl-dithiobiurets (II) were obtained, according to the literature data, by heating "xanthane hydride" with aromatic amines. The yields ranged from 60 to 65%. Melting point of phenyldithiobiuret 179-184° [12]), of p-chlorophenyldithiobiuret 167-168° (163-164° [14], 179-180° [12]), of p-anisyldithiobiuret 173-174° (173-174° [12]), of o-anisyldithiobiuret 142-143° (143-144° [12]), of p-tolyldithiobiuret 170-171° (173-174° [12]), and of o-tolyldithiobiuret 167° (159° [15]).

The 5-arylimino-3-imino-1,2,4-dithiazolidines (arylthiurets) (III) were obtained by the oxidation of the corresponding dithiobiurets with iodine in alcohol medium, using the Fromm method [16], and were isolated as the hydriodides. The products were purified by recrystallization from alcohol. The yields ranged from 70 to 90%. Melting points of hydriodic acid salts: phenylthiuret (IIIa) 157-158°, p-chlorophenylthiuret (IIIb) 229-230°, p-anisylthiuret (IIIc) 180-182° (182° [17]), o-anisylthiuret (IIId) 198-199° (199-200° [17]), p-tolylthiuret (IIIe) 217-218°, and o-tolylthiuret (IIIf) 143-145°.

Analysis Results.

(IIIa) – Found %: N 12.54. $C_8H_7N_3S_2 \cdot HI$. Calculated %: N 12.43. (IIIb) – Found %: N 11.35. $C_8H_6N_3S_2Cl \cdot HI$. Calculated %: N 11.30. (IIIc) – Found %: N 12.07. $C_9H_9N_3S_2 \cdot HI$. Calculated %: N 11.96. (IIId) – Found %: N 11.96. $C_9H_9N_3S_2 \cdot HI$. Calculated %: N 11.96.

Potassium salts of N-aryl-N'-cyanoisothioureas (IV). The thiuret hydriodide (III) (0.015 mole) was added with stirring to an ice cooled solution of 1 g of potassium hydroxide in 20 ml of water. After 30 minutes the deposited sulfur was filtered, and the filtrate was evaporated. The potassium salts (colorless needles) were obtained in quantitative yield. Melting points: (IVa) 201-202°, (IVb) 240-241°, (IVc) 218-226°, and (IVe) 232-234°.

Formation of precipitates in reaction of potassium salts with ions of some metals. To 2 ml of a 0.25 N solution of metal salt was added 2-3 drops of 0.1 M solutions of the investigated potassium salts of cyanamidodithiocarbonic acid (VII) and N-aryl-N'-cyanothioureas (IV). The characteristics of the obtained precipitates are given in Table 1.

N-phenyl-N'-cyanothiourea (Va). A suspension of 0.6 g of potassium salt (IVa) in 3 ml of ice-cooled 1 N hydrochloric acid was prepared. The suspension was filtered, and washed with cold water. We obtained 0.2 g of a yellow precipitate with m. p. 95-111° (decompn.). The substance is very soluble in hot alcohol. It decomposes when heated with water to a tarry product.

N-(p-chlorophenyl)-N'-cyanothiourea (Vb). A suspension of 0.85 g of potassium salt (IVb) in 3.2 ml of ice-cooled 1 N hydrochloric acid was prepared. The colorless crystalline precipitate was filtered and washed with cold water. The substance rapidly turns yellow in the air, m. p. 108-112° (decompn.) (157-158° [11]). When boiled in a mixture of alcohol and benzene it is converted to a crystalline substance of not investigated structure with m. p. 270-275° (decompn.). Treatment of the moist precipitate with 5% potassium hydroxide solution gave the potassium salt. The water solution of the potassium salt was evaporated to dryness on the

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* We wish to thank E. I. Chertkova (Sverdlovsk Tuberculosis Institute) for testing the indicated compounds.

water bath, and the residue was heated for 1 hour with methyl iodide in alcohol medium. We obtained 0.6 g of the methyl ester of N-(p-chlorophenyl)-N'-cyanothiourea (VIb) as a crystalline product with m. p. 184°, not depressing the melting point when mixed with the methyl ester obtained from the potassium salt of N-(p-chlorophenyl)-N'-cyanoisothiourea (IVb).

Methyl esters of N-aryl-N'-cyanoisothioureas (VI). The N-aryl-N'-cyanoisothiourea potassium salt (IV) (0.02 mole) was heated for 1 hour with 0.03 mole of methyl iodide in 2-3 ml of alcohol. The solution was evaporated to dryness, made turbid with several milliliters of warm water, filtered, and the precipitate washed with water. All of the obtained esters crystallized readily from ethyl alcohol as colorless plates. The yields ranged from 42 to 52%. The melting points and analysis data are given in Table 2.

TABLE 1

Metal Salt	Starting compounds			
	(VII)	(IVa)	(IVb)	(IVc)
$Hg(NO_3)_2$	Colorless precipitate	Small amount of yellow precipitate, rapidly becoming colorless	Yellow precipitate, rapidly becoming colorless	Yellow precipitate, rapidly becoming colorless
$Zn(NO_3)_2$	Colorless precipitate	Colorless precipitate	Colorless precipitate	Colorless precipitate
$CD(NO_3)_2$	Colorless precipitate	Colorless precipitate	Colorless precipitate	Colorless precipitate
$Hg_2(NO_3)_2$	Brown precipitate	Brown precipitate	Light brown precipitate	Light brown precipitate
$Cu(NO_3)_2$	Brown precipitate Solution becomes green	Light-green precipitate, turning to a brown solution green	Brown precipitate turning to a light-green. Solution green.	Light-green precipitate. Solution green
$Bi(NO_3)_3$	Trace amount of yellow precipitate, turning orange	Brown precipitate, turning to an apricot-colored precipitate	Small amount of brown precipitate	Small amount of brown precipitate, turning to an apricot-colored precipitate. Solution yellow
$Pb(Ac)_2$	Yellow precipitate	Colorless precipitate	Yellow precipitate, turning colorless	Bright yellow precipitate, becoming colorless immediately
$ZrSO_4$	Slight turbidity	A colorless precipitate gradually appears	Slight turbidity, a colorless precipitate deposits gradually	Slight turbidity, a colorless precipitate deposits gradually
$AgNO_3$	Yellow precipitate, turning to a brown	The same as for compound (VII)		

Methyl ester of N-anisyl-N'-cyanoisothiourea (IVc). The dimethyl ester of cyanamidodithiocarbonic acid (m. p. 56-57°) (0.44 g), obtained by the procedure of [9], was heated on the water bath for 10 minutes with a solution of 0.37 g of p-anisidine in 3 ml of alcohol (sharp odor of mercaptan). The obtained precipitate after cooling was filtered and washed with a small amount of alcohol. Yield 0.5 g (76%), m. p. 181-182°. It fails to depress the melting point when mixed with the methyl ester of N-anisyl-N'-cyanoisothiourea (VIc), obtained from the potassium salt of N-anisyl-N'-isocyanothiourea (IVc).

Reaction of "xanthane hydride" with α-aminopyridine. A mixture of 3 g (0.02 mole) of "xanthane hydride" and 3.76 g (0.04 mole) of α-aminopyridine in 10 ml of alcohol was heated for 1 hour on the boiling water bath. The deposited sulfur was filtered and from the filtrate after cooling was isolated 5.1 g (84%) of the thiocyanic acid salt of α-aminopyridine. Colorless prisms from alcohol, m. p. 115-116°.

TABLE 2

Compounds	Empirical formula	Melting point	Found (%)		Calculated (%)	
			N	S	N	S
(VIa)	$C_9H_9N_3S$	185—186°	21.74	16.86	22.00	16.75
(VIb)	$C_9H_8N_3SCl$	184—185 (decompn.)	18.37	13.88	18.61	14.21
(VIc)	$C_9H_{11}N_3SO$	181—182	19.10	14.37	19.01	14.41
(VIe)	$C_{10}H_{11}N_3S$	148—149	20.77	—	20.48	—

Found %: N 26.88. $C_6H_7N_3S$. Calculated %: N 27.41.

When reacted with sodium hydroxide solution in the cold the substance yields the free α-aminopyridine and sodium thiocyanate. In a similar manner the reaction of α-aminopyrimidine with "xanthane hydride" gave a 77% yield of the thiocyanic acid salt of α-aminopyrimidine, obtained as colorless prisms; after recrystallization from alcohol, m. p. 137-138°.

Found %: N 36.15. $C_6H_6N_4S$. Calculated %: N 36.33.

Reaction of p-chlorophenyldithiobiuret with α-aminopyridine. A mixture of 3 g (0.012 mole) of p-chlorophenyldithiobiuret and 1.15 g (0.012 mole) of α-aminopyridine was heated for 1 hour in an oil bath at 125-130°. Within 10-15 minutes after the start of heating a test sample of the melt gave a distinct test for thiocyanic acid (red color with ferric chloride solution). At the end of heating the melt was shaken with 20 ml of water, filtered, and the precipitate on the filter washed well with water until all of the thiocyanic acid salt of α-aminopyridine had been removed (test with ferric chloride solution). Evaporation of the filtrate and wash waters led to obtaining 1.75 g (95%, based on taken α-aminopyridine) of the thiocyanate of α-aminopyridine, obtained as crystals with m. p. 115-116°. Three recrystallizations of the water-insoluble residue (0.60 g) from alcohol gave: 0.25 g of p-chlorophenylthiourea with m. p. 176-177° (175° [18]) and 0.1 g of N,N'-bis(p-chlorophenyl)thiourea with m. p. 168-170° (166-168° [18]).

Analysis results for p-chlorophenylthiourea and N,N'-bis(p-chlorophenyl)thiourea. Found %: N 14.65. $C_7H_7N_2SCl$. Calculated %: N 15.06. Found %: N 10.02. $C_{13}H_{10}N_2SCl_2$. Calculated %: N 9.46.

SUMMARY

1. The potassium salts and methyl esters of the iso forms of N-aryl-N'-cyanothioureas were obtained. Five-imino-3-thio-1,2,4-dithiazolidine ("xanthane hydride") was used as the starting material.

2. It was established that α-aminopyridine and α-aminopyrimidine, in contrast to aromatic amines, cleave "xanthane hydride" to yield thiocyanic acid salts of heterocyclic amines, and not dithiobiurets.

3. It was shown that the potassium salts of cyanamidodithiocarbonic acid and N-aryl-N'-cyanoisothioureas form water-insoluble precipitates with various metals.

4. The in vitro testing of the potassium salts of N-aryl-N'-cyanoisothioureas revealed that they were inactive toward tubercle bacillus.

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Received December 20, 1956

MECHANISM OF THE REACTION OF TRANSAMINATION IN THE β-DIALKYLAMINOPROPIONITRILE SERIES

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Relative to the reaction discovered by us [1], and later by Bauer, Cymerman and Sheldon [2],* for alkyl-aryl transamination in the β-dialkylaminopropionitrile series

$$(Alk)_2NCH_2CH_2CN + Ar\overset{+}{N}H_3\overset{-}{An} \rightleftharpoons ArNHCH_2CH_2CN + (Alk)_2\overset{+}{N}H_2\overset{-}{An}$$

differences exist as to the mechanism of the process that takes place here. This reaction, leading to the formation of the β-arylaminopropionitrile, can be accomplished by two procedures.

1. The elimination of the dialkylamine with subsequent addition of the aromatic amine to acrylonitrile in the presence of the dialkylammonium salt, functioning as an acid catalyst.

$$(Alk)_2NCH_2CH_2CN + Ar\overset{+}{N}H_3\overset{-}{An} \rightarrow (Alk)_2\overset{+}{N}HCH_2CH_2CN\overset{-}{An} + ArNH_2$$

$$(Alk)_2\overset{+}{N}HCH_2CH_2CN\overset{-}{An} \rightarrow (Alk)_2NH + [\overset{+}{C}H_2CH_2CN]\overset{-}{An};$$

$$[\overset{+}{C}H_2CH_2CN]\overset{-}{An} \rightarrow HAn + CH_2{=}CH{-}CN$$

$$(Alk)_2NH + HAn \rightarrow (Alk)_2\overset{+}{N}H_2\overset{-}{An};$$

$$CH_2{=}CH{-}CN + ArNH_2 \xrightarrow{\substack{\text{catalyst}\\ [(Alk)_2\overset{+}{N}H_2\overset{-}{An}]}} ArNHCH_2CH_2CN$$

When a β-dialkylaminopropionitrile is reacted with a salt of an aromatic amine (hydrochloride, sulfate, acetate, etc.) a proton migrates to the β-dialkylaminopropionitrile as being the stronger base. The N-β-cyanoethyl-N,N-diethylammonium ion formed in this manner is unstable, due to the polarization of its bonds [3], and decomposes into diethylamine and acrylonitrile; the latter adds aromatic amine in the presence of an acid catalyst, when the dialkylammonium salt is at the reaction temperature.

2. The second procedure proposed is nucleophilic displacement or some similar reaction, where the hydrogen of the aromatic amine participates in the formation of the cleaved dialkylamine, i.e., a direct replacement of the dialkylamino group by the aromatic amine.

$$\overset{-}{An}(Alk)_2\overset{+}{N}HCH_2CH_2CN + ArNH_2 \rightarrow \overset{-}{An}Ar\overset{+}{N}H_2CH_2CH_2CN + (Alk)_2NH \rightarrow$$

$$\rightarrow ArNHCH_2CH_2CN + \overset{-}{An}\overset{+}{N}H_2(Alk)_2$$

In opposition to this we believe that the reaction proceeds by the first scheme, i.e., cleavage of the N-β-cyanoethyl-N,N-dialkylammonium ion occurs first and this is followed by the addition of the aromatic amine to either the formed acrylonitrile or the carbonium ion.

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* Our paper [1] was received by the editor on April 4, 1949, and that of the British authors [2] on June 14, 1951.

We had found [1] that the heating of β-diethylaminopropionitrile hydrochloride with aniline, or of the free base of the former with aniline hydrochloride, gives β-phenylaminopropionitrile in 64-67% yield. It proved that the hydrochloride of β-diethylaminopropionitrile is unstable and when heated decomposes into diethylamine hydrochloride and acrylonitrile. We ran the decomposition of the β-diethylaminopropionitrile hydrochloride in a Claisen flask with removal of the cleaved acrylonitrile by distillation, which was obtained by us in 77% yield.

Somewhat later Cymerman-Craig and co-workers [4], disputing this data, heated β-diethylaminopropionitrile hydrochloride in a flask under reflux and isolated 73% of unchanged β-diethylaminopropionitrile hydrochloride. Here they assumed that they had the conditions employed for the transamination reaction and concluded that the hydrochloride of β-diethylaminopropionitrile is stable. We are of the opinion that such a conclusion is without basis. The decomposition of β-diethylaminopropionitrile hydrochloride when heated is a reversible reaction

$$\bar{Cl}(C_2H_5)_2\overset{+}{N}HCH_2CH_2CN \rightleftarrows \bar{Cl}(C_2H_5)_2\overset{+}{N}H_2 + CH_2{=}CH{-}CN$$

and consequently it can be shifted in either direction depending on the concentration of the reactants in the reaction mixture. If acrylonitrile is removed from the reaction sphere (either by distillation or in the presence of aniline by reaction with the latter), then the reaction is shifted to the right. If the formed acrylonitrile and diethylamine hydrochloride remain in the reaction mixture, then the decomposition of the diethylaminopropionitrile hydrochloride proceeds only to establishing equilibrium. This conclusion is supported by experimental data. We found that diethylamine hydrochloride adds to acrylonitrile in anhydrous medium, i.e., under the conditions of the transamination reaction. By heating under reflux, Cymerman-Craig and co-workers [4] created conditions for establishing equilibrium in the reaction mixture at the experiment temperature, and this is the reason for their being able to obtain only a 27% decomposition of β-diethylaminopropionitrile hydrochloride.

That the mechanism for the discussed reaction corresponds to the first scheme is also supported by our experiment of heating aniline hydrochloride and β-diethylaminopropionitrile at 160°, run under conditions assuring the removal of volatile products. It was found that here the yield of cleaved acrylonitrile is only 47% (instead of 77%), and β-phenylaminopropionitrile is formed in 34% yield. These data permit the following explanation of the transformations that take place here: acrylonitrile, formed in the decomposition of the β-diethylaminopropionitrile, is partially removed by distillation and partially (possibly as a carbonium ion) adds aniline. This is the reason why only 47% of the acrylonitrile is removed by distillation, instead of the 77% obtained when the reaction is run in the absence of aniline. The obtained data clearly show that the process goes by the first scheme.

The instability of the hydrochloride of β-diethylaminopropionitrile and its tendency to decompose also appear at moderate temperatures, for example, when aqueous solutions of this salt are heated. It was found that the reaction for alkyl-aryl transamination can also proceed in water medium; here we obtained β-phenylaminopropionitrile in 50% yield. The heating of a water solution of β-diethylaminopropionitrile with removal of the volatile products by distillation also leads to decomposition of the taken nitrile into acrylonitrile and diethylamine (58%). These data also contradict the statement of Cymerman-Craig and co-workers [4] that β-diethylaminopropionitrile hydrochloride is stable.

As further evidence in support of the substitution mechanism (Scheme 2) the authors of [4] cite the fact that an aromatic amine hydrochloride when heated with acrylonitrile does not form the β-arylaminopropionitrile, whereas under the same conditions the hydrochloride of an aromatic amine reacts with β-diethylaminopropionitrile to give the β-arylaminopropionitrile in 78% yield. This conclusion also proves to be invalid, since we had established that the hydrochloride of an aromatic amine does not react with acrylonitrile in anhydrous medium and at low temperature (at the boiling point of acrylonitrile) for the reason that a proton is absent under these conditions, being a catalyst for the reaction (acrylonitrile is not a dissociating medium for an aromatic amine hydrochloride). The presence of an acid catalyst, for example diethylamine hydrochloride, suffering thermal dissociation under the experimental conditions (140-180°), assures the entrance of a proton into the reaction mixture.

It was found by us that an aromatic amine hydrochloride can add to acrylonitrile even when the heating is in aqueous medium, since apparently an aqueous medium, creating conditions for dissociation, assures the presence of a proton in the reaction mixture.

The possibility established by us of running the alkyl-aryl transamination reaction in aqueous medium and the fact that acrylonitrile adds to an aromatic amine hydrochloride in aqueous medium do not agree with the conclusions [4] that the substitution mechanism prevails here.

In a later paper [5] some data are presented, showing the relationship between the basicity of the aromatic amine and the yield of β-arylaminopropionitrile in the alkyl-aryl transamination reaction. The authors make the statement that the greater the basicity of the amine, the higher the yield of β-arylaminopropionitrile. The authors link this fact to the S_N2 mechanism [6] of nucleophilic displacement. However it should be mentioned, as had been shown by us earlier [7], that in the direct addition of aromatic amines to acrylonitrile the higher yields of β-arylaminopropionitriles are also associated with a greater basicity of the starting aromatic amine.

Interesting data, however not supporting the arguments of the indicated authors [5], were obtained by the latter when they introduced β-diethylamino-α-dimethylpropionitrile as one of the components in the discussed reaction. This compound, for structural reasons incapable of eliminating diethylamine and forming a double bond, is practically inert toward p-anisidine (the yield of product with unknown structure is a total of only 0.1%). In our opinion, this fact also strongly supports the theory that the reaction proceeds by way of elimination.

It was shown by Bauer and co-workers [2] that the alkyl-aryl transamination reaction does not go in the presence of BF_3, an acid catalyst. This circumstance also supports the conclusion that a proton-cleaving catalyst is necessary for the studied reaction.

Brewster and Eliel [8], discussing the alkylation mechanism of ammonium salts, came to the conclusion that the mechanism of the reaction consists in the cleavage of secondary amine with the formation of an unsaturated compound, which then adds the alkylating substance. They also consider the possibility of nucleophilic displacement less probable on the basis that the removal of a proton from the ammonium salt should proceed more easily than the displacement of a dialkylamine molecule.

Relative to the experiments made by the indicated authors [4] with deuterium, undertaken by them to prove the nucleophilic mechanism of the discussed reaction, it should be stated that the absence of analysis data for the deuterium content of the β-arylaminopropionitrile, and also the inadequate description of the experiments on the study and analysis of the diethylamine and water, unfortunately do not permit arriving at a conclusion as to the reliability of the arguments offered by Cymerman-Craig and co-workers [4].

Summarizing all of the above, we believe that the reaction of alkyl-aryl transamination in the β-dialkylaminopropionitrile series proceeds rather by way of cleavage of the dialkylamine and subsequent addition of the aromatic amine to the formed acrylonitrile (or to the carbonium ion) than by way of nucleophilic displacement.

EXPERIMENTAL

Alkyl-aryl transamination. a) A mixture of 3.3 g (0.026 mole) of β-diethylaminopropionitrile, 2.5 g (0.026 mole) of aniline and 3.1 g (0.050 mole) of glacial acetic acid was heated in a flask under reflux for 2 hours at 160° in a metal bath. The mixture was treated with alkali, and the separated oil was extracted with benzene. After removal of the benzene by distillation, two fractions were isolated: aniline with β-phenylaminopropionitrile as impurity, b. p. up to 100° at 5 mm, and β-phenylaminopropionitrile, b. p. 153-155° at 4 mm; yield 1.8 g (56.2 %), m. p. 49° (from alcohol).

b) A mixture of 12.6 g (0.1 mole) of β-diethylaminopropionitrile and 12.95 g (0.1 mole) of aniline hydrochloride was placed in a Claisen flask, fitted with two thermometers (one in the reaction mixture, and the other in the vapors) and a descending condenser. The flask was heated in a metal bath at 180° for 1.5 hours (reaction mixture 160°; vapor temperature 78-82°), at which time 2.2 ml of acrylonitrile distilled off (b. p. 78°, n_D^{20} 1.3930 on redistillation). To the residue in the Claisen flask was added 5.0 g (0.125 mole) of powdered sodium hydroxide, the mixture heated on the boiling water bath, and the diethylamine with aniline impurity distilled off at 56-74° (7.0 ml). The presence of aniline in the distillate was qualitatively shown by testing for primary amine (diazotization and coupling with β-naphthol). After drying over NaOH the mixture was fractionally distilled, the diethylamine distilling at 56° (5.5 ml). Water was added to the residue in the flask, and the obtained oil was extracted with benzene. After removal of the benzene by distillation the residue was vacuum-distilled. The aniline distilled first (2.9 g), b. p. up to 120° at 20 mm, and then the β-phenylaminopropionitrile with b. p. 178-180° at 10 mm; yield 5.1 g (34.9%, based on taken β-diethylaminopropionitrile); m. p. 49° (from alcohol).

c) A mixture of 3.5 g (0.025 mole) of β-diethylaminopropionitrile and 3.25 g (0.025 mole) of aniline hydrochloride was heated in water (5 ml) at the boil. After the usual treatment we isolated from the reaction mixture: aniline with β-phenylaminopropionitrile as impurity, b. p. up to 110° at 24 mm (1.0 g), and β-phenylaminopropionitrile with b. p. 196° at 24 mm; yield of the latter 1.9 g (52 %), m. p. 50° (from alcohol).

Addition of aniline hydrochloride to acrylonitrile. a) In anhydrous medium. A mixture of 6.5 g (0.050 mole) of aniline hydrochloride and 5.3 g (0.1 mole) of acrylonitrile was heated at the boil for 14 hours. The mixture was treated with dilute caustic solution, and the obtained oil was extracted with benzene. After distilling off the benzene we isolated 2.8 g of aniline, b. p. up to 100° at 4 mm. No residue was left in the flask.

b) In water medium. A mixture of 13.0 g (0.1 mole) of aniline hydrochloride and 5.5 g (0.105 mole) of acrylonitrile in 25 ml of water was heated at the boil for 14.5 hours. After the usual treatment we obtained 7.0 g of aniline and 1.6 g (11%) of β-phenylaminopropionitrile with b. p. 153° at 3 mm and m. p. 49° (from aqueous alcohol).

Conditions for the formation and decomposition of β-diethylaminopropionitrile. Differing from the known conditions for the addition of free diethylamine to acrylonitrile [9, 10], we were able to add both diethylamine hydrochloride and the acetate to acrylonitrile.

a) A mixture of 7.3 g (0.1 mole) of diethylamine, 8.0 g (0.15 mole) of acrylonitrile and 6.0 g (0.1 mole) of glacial acetic acid was heated for 3 hours at the boil. After vacuum-distillation of the volatile products on the water bath and the usual treatment of the residue we obtained 7.4 g (58.7%) of β-diethylaminopropionitrile with b. p. 95-97° at 21 mm.

b) A mixture of 5.5 g (0.05 mole) of diethylamine hydrochloride and 5.3 g (0.1 mole) of acrylonitrile was heated at the boil for 10 hours. We obtained 2.5 g (39.6%) of β-diethylaminopropionitrile with b. p. 92-93° at 18 mm.

c) A solution of 5.5 g (0.05 mole) of diethylamine hydrochloride in 5 ml of water and 3.0 g (0.056 mole) of acrylonitrile was heated at the boil for 14 hours. We obtained 1.5 g (23.8%) of β-diethylaminopropionitrile with b. p. 110-112° at 42 mm.

Decomposition of dry β-diethylaminopropionitrile hydrochloride with removal of volatile products by distillation. The yield of distilled acrylonitrile under the indicated conditions (160-190°) was 77% [1].

Decomposition of aqueous solution of β-diethylaminopropionitrile hydrochloride. A solution of 8.1 g (0.05 mole) of β-diethylaminopropionitrile in 5 ml of water was heated in a Claisen flask with slow removal of water by distillation. Water was added to the mixture during distillation at such a rate that the concentration of the solution remained constant. A total of 20 ml of water was added, while the amount distilled off was 18 ml. The amount of acrylonitrile (b. p. 76°) removed with the water was 1.5 ml. The residue in the flask after evaporation to dryness was treated with 2 g of powdered NaOH. The mixture was heated on the water bath, and here 3.0 ml (2.1 g, 58.3%) of diethylamine with b. p. 56° was collected by distillation.

SUMMARY

1. The mechanism of our discovered [1] reaction of alkyl-aryl transamination in the β-dialkylaminopropionitrile series consists of the cleavage of the dialkylamino radical from the latter, followed by addition of the arylamine to the formed acrylonitrile in the presence of a proton.

2. The opinion held by some authors [4] that the indicated reaction is one of direct nucleophilic displacement of the dialkylamino group by the arylamine radical stands in contradiction to our experimentally established cleavage of acrylonitrile (47%) under the conditions of this reaction, and also to the cleavage of the latter in an amount of 77% when diethylaminopropionitrile hydrochloride is heated in the absence of aniline.

3. The statement made by the same authors that it is necessary to have diethylamine present in order for aromatic amine hydrohalides to add to acrylonitrile is not correct, since the indicated addition does take place in the absence of diethylamine, under the influence of acid catalysts.

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Received November 22, 1956

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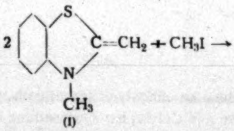
*Original Russian pagination. See C. B. Translation.

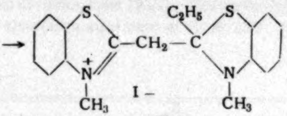
ON THE PRODUCTS OF REACTION BETWEEN METHYLENE BASES OF BENZOTHIAZOLE AND BENZSELENAZOLE AND ALKYL HALIDES

F. S. Babichev and A. I. Kiprianov

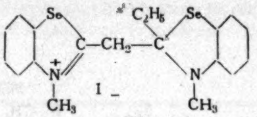
Towards the end of 1955 was published the abstract of a patent by Larive and Collet [1] in which the authors described adducts of methyl iodide to 3-methyl-2-methylenebenzthiazoline (I) and 3-methyl-2-methylenebenzselenazoline (II), and the novel triple nuclear dyes obtained from these products. According to Larive and Collet the action of methyl iodide on compound (I) gives rise to the formation of the salt (III).



(I)



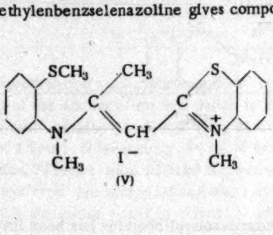
(III)



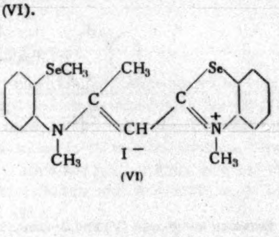
(IV)

Similarly, from methyl iodide and compound (II) is obtained the corresponding derivative of benzselenazole (IV).

It must be noted, however, that the reaction of methylene bases derived from benzothiazole, benzselenazole and thiazole with alkyl halides has been investigated by us in detail as far back as 1950 [2], and that the structure assigned to these products by Larive and Collet is incorrect. In fact, the reaction of methyl iodide with 3-methyl-2-methylenebenzthiazoline results in the formation of compound (V), while the reaction with 3-methyl-2-methylenbenzselenazoline gives compound (VI).



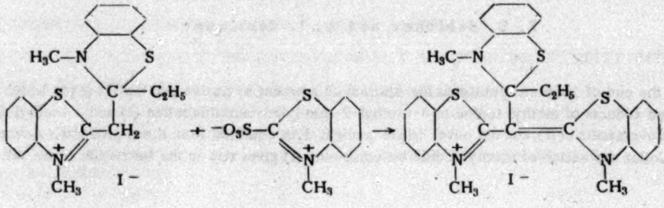
(V)



(VI)

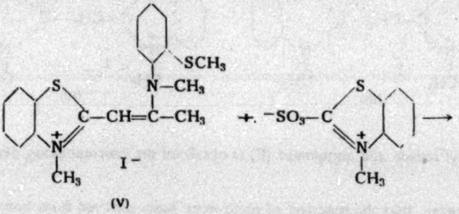
Structures of compounds (V) and (VI) have been confirmed by investigation of their properties and of those of the products of their hydrolysis. Compounds of similar structures have been prepared by Babichev by the interaction of methylene bases derived from benzothiazole with α-haloketones, esters of α-haloacids, halogen substituted acid anhydrides and cyanogen bromide [3].

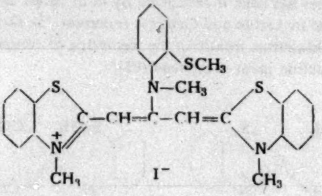
Larive and Collet have utilized the adducts of methyl iodide to methylene bases in the synthesis of triple-nuclear monomethinecyanines, allegedly through the intermediate stage of the formation of N-methyl-2-benzothiazolesulfobetaine [4]. Having assigned an incorrect structure to the starting materials the authors have, quite naturally, also assigned an incorrect structure to the dyes obtained. According to Larive and Collet, the formation of these dyes proceeds according to the following scheme (taking the benzothiazole derivative as example):


(III)

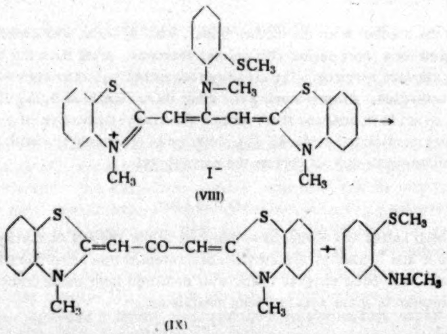
(VII)

In reality, however, the reaction follows an entirely different path, the resultant product being not a monomethinecyanine, as supposed by Larive and Collet, but a trimethine dye substituted in the chain (VIII):


(V)


(VIII)

The reaction between compound (V) and 3-methyl-2-benzthiazolesulfobetaine has been investigated by us in some detail. The orange-colored dye — the product of this reaction — is easily hydrolyzed on heating with caustic potash. As a result there is formed a yellow-colored substance which melts at 339° with decomposition and which was found to be identical with the authentic ketone (IX) [5] (see below). This ketone has been prepared by us and did not depress the melting point in mixture with the product of hydrolysis. The second compound isolated from the hydrolysate was the methyl ether of o-methylaminothiophenol. The hydrolysis of the dye obtained by Larive and Collet proceeds, therefore, according to the following equation:

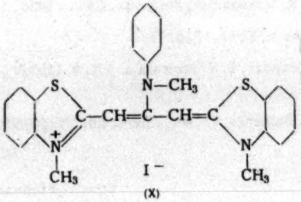


(VIII)

(IX)

These compounds cannot, obviously, be obtained on hydrolysis of a dye having the structure (VII).

Thiocarbocyanines with arylamino groups in the meso position of the chain are well known [6] and resemble in properties compound (VIII). The absorption peak of the dye (VIII) in alcoholic solution lies at 493 mμ, while the absorption maximum of the dyestuff (X), similar in structure to compound (VIII), lies at 497 mμ.



(X)

EXPERIMENTAL

3,3'-Dimethyl-9-[(o-methylmercapto-N-methyl)-phenylamino]-thiocarbocyanine iodide (VIII). A mixture of 4.68 g of the adduct of methyl iodide to 3-methyl-2-methylenebenzthiazoline (I) [7], 3.6 g of N-methyl-2-benzthiazolesulfobetaine [1, 4] and 1.2 g of triethylamine in 30 ml of absolute alcohol was refluxed on a water bath for 1 hour. Subsequently, 60 ml of ether was added to the reaction mixture. The crystals which separated within 24 hours were filtered off, washed with ether and recrystallized from 140 ml of 50% methanol. Yield of the dye after two recrystallizations, 1.85 g (30%). Reddish-orange crystals, m. p. 247° with decomposition (uncorr.); absorption peaks in alcohol at 399 and 493 mμ.

Found %: N 6.82, 6.69; I 20.96, 20.88. $C_{27}H_{26}N_3S_3I$. Calculated %: N 6.83; I 20.61.

Two g of the pure dye was heated for 40 minutes with a solution of 0.5 g of caustic potash in 5 ml of water and 40 ml of alcohol. There separated large yellow needles. After cooling the suspension, the crystals were filtered off, and washed with alcohol, water, followed by a second washing with alcohol and finally with ether. There was obtained 0.65 g of a yellow-colored substance melting at 339° with decomposition (corr.). After a second recrystallization the melting point did not change. Mixture of the substance with 1,3-bis-(3'-methyl-benzothiazolinylidene-2')-propanone (IX), prepared according to Kendall [5], did not depress the melting point. To the mother liquor was added 1 ml of conc. hydrochloric acid. The yellow crystals which separated were filtered off, heated with 5 ml of pyridine, again filtered and washed with ether. Another 0.2 g of the substance was obtained, m. p. 338°, with decomposition. Thus, the total yield of ketone (IX) was 0.85 g (87%).

After removing the alcohol from the mother liquor, 8 ml of water was added to the residue, after which the solution was refluxed for a short period with animal charcoal. After filtering and cooling, sodium hydroxide solution was added to alkaline reaction. The oil which separated was extracted with ether and the ether extract dried over potassium hydroxide. After removing the ether there remained 0.35 g of a yellow oil. On acting on the latter with acetyl chloride in benzene there formed the acetyl derivative of o-methylmercapto-N-methylaniline as long colorless needles, m. p. 81-82° [7]. Mixture of the substance with an authentic sample obtained from N-methylaminothiophenol did not depress the melting point.

SUMMARY

The structure which Larive and Collet have assigned to the adducts of methyl iodide to 3-methyl-2-methylenebenzthiazoline and 3-methyl-2-methylenebenzselenazoline have been found to be incorrect. Likewise, incorrect structures have been assigned to the dyes obtained from these compounds. In the present investigation the true structure of these dyes has been established.

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Kiev State University

Received January 2, 1957

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*Original Russian pagination. See C. B. Translation.

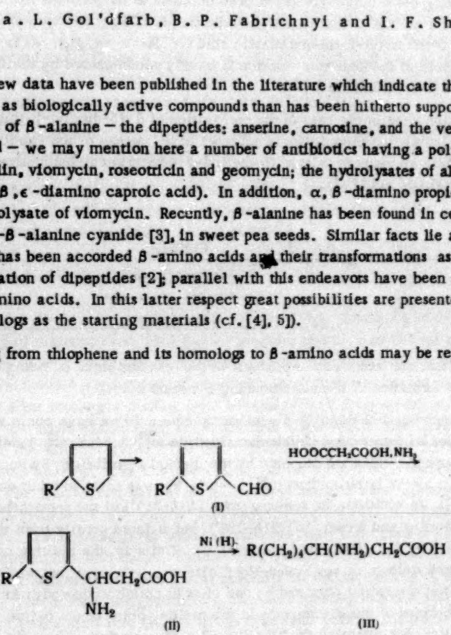
SYNTHESIS OF ALIPHATIC AMINO ACIDS FROM THIOPHENE DERIVATIVES

II. SYNTHESIS OF β-AMINO ACIDS

Ia. L. Gol'dfarb, B. P. Fabrichnyi and I. F. Shalavina

In recent years new data have been published in the literature which indicate that β-amino acids play a more significant role as biologically active compounds than has been hitherto supposed. In addition to the well-known derivatives of β-alanine – the dipeptides: anserine, carnosine, and the very important growth promotor, pantothenic acid – we may mention here a number of antibiotics having a polypeptide structure such as streptotricin, streptolin, viomycin, roseotricin and geomycin; the hydrolysates of all the latter compounds contain β-lysine [1, 2] (β,ε-diamino caproic acid). In addition, α, β-diamino propionic acid has been detected in the acid hydrolysate of viomycin. Recently, β-alanine has been found in co-enzyme "A" and, in the form of glutaminyl-β-alanine cyanide [3], in sweet pea seeds. Similar facts lie at the root of the increased interest which has been accorded β-amino acids and their transformations as, for example, reactions which lead to the formation of dipeptides [2]; parallel with this endeavors have been made to find new ways of synthesizing these amino acids. In this latter respect great possibilities are presented through the use of thiophene and its homologs as the starting materials (cf. [4], 5]).

The path leading from thiophene and its homologs to β-amino acids may be represented by the following scheme:



The second stage of this process consists of the condensation of the aldehyde (I) with malonic acid and ammonia to give the β-amino acid according to the well-known method developed by V. M. Rodionov and co-workers [6, 8] a β-amino acid containing thiophene was first synthesized by the method of Mamaev, Suvorov and Rokhlin [9]. The final stage of the reaction is reduction and desulfurization* in the presence of Raney nickel under conditions described earlier [4, 5]. The preparation of β-amino acids by this method affords all the possible synthetic variants already discussed in our recent communications [4, 5] dealing with the synthesis of amino acids of other types, namely, chain lengthening and preparation of amino acids with branched chains.

It will be seen from the scheme shown above that an amino acid with a branched structure will result if the alkyl substituent or aldehydic group are in positions 3 or 4, as also when the substituent in position 5 has a branched structure.

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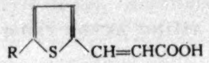
*For brevity's sake this stage of the process will be referred to as hydrogenolysis.

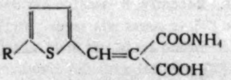
Putting our program of investigation into effect we have, starting from 2-thiophenaldehyde (I, R = H), 5-methyl-2-thiophenaldehyde (I, R = CH_3), 5-ethyl-2-thiophenaldehyde (I, R = C_2H_5) and 5-tert-butyl-2-thiophenaldehyde (I, R = tert-C_4H_9), prepared β-(2-thienyl)-β-aminopropionic (II, R = H), β-(5-methyl-2-thienyl)-β-aminopropionic (II, R = CH_3), β-(5-ethyl-2-thienyl)-β-aminopropionic (II, R = C_2H_5), and β-(5-tert.-butyl-2-thienyl)-β-aminopropionic (II R = tert.-C_4H_9) acids in yields varying from 25 to 41%. The last three acids have not been described previously. The acids have been characterized also in the form of their various derivatives.



(IV)

Unsaturated acids having the structure (IV) have been obtained as by-products namely: β-(2-thienyl)-acrylic acid (IV, R = H), β-(5-methyl-2-thienyl)acrylic acid (IV, R = CH_3), β-(5-ethyl-2-thienyl)acrylic acid (IV, R = C_2H_5) and β-(5-tert-butyl-2-thienyl)acrylic acid (IV, R = tert-C_4H_9). As is well-known, synthesis of amino acids under conditions of the Rodionov reaction is usually accompanied by the formation of the corresponding unsaturated acids (see, for example [9]).

On reducing the reaction time in the case of the preparation of β-(5-methyl-2-thienyl)-β-aminopropionic and β-(5-ethyl-2-thienyl)-β-aminopropionic acids we have, instead of the expected β-amino acids, obtained in good yield the acid ammonium salts of (5-methyl-2-thienyl)methylenemalonic acid (V) and (5-ethyl-2-thienyl)methylenemalonic acid (VI).



(V) R=CH_3; (VI) R=C_2H_5.

These salts may represent the intermediate products of the reaction since on being heated with ammonium acetate they give rise to the formation of the corresponding β-amino acids.

In synthesizing β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid we have come across some unexpected features. The refractive index of 5-tert-butyl-2-thiophenaldehyde (n_D^{20} 1.5462, n_D^{22} 1.5451, n_D^{25} 1.5436) obtained from 2-tert-butyl-thiophene which we prepared by the method described by Sy, Buu-Hoi and Xuong [10] differed from the value given by the latter authors (n_D^{22} 1.5495), but was close to other data published (n_D^{25} 1.5428 [11], n_D^{25} 1.5441 [12]). In addition, the melting point (216-217°) of the semicarbazone of our aldehyde was close to that given by Messina and Brown [13] (215-216°), but differed greatly from the melting point (249°) of the semicarbazone obtained by Buu-Hoi and co-workers [10]. Similarly, the melting point (118-119°) of the oxime of our aldehyde differed from that given by Buu-Hoi [10] for this derivative, but was almost identical with the melting point (121-122°) of the oxime obtained by one of us in collaboration with Antik and Konstantinov [14]. In order to explain the cause of this discrepancy in the melting point of the oxime we decided to alter the conditions of its preparation, but retaining the alkaline pH of the solution. The oxime obtained in this way had a melting point of 73-74° and is probably the geometrical isomer of the oxime with a melting point of 118-119°. Buu-Hoi and co-workers do not describe the conditions of preparation of the oxime melting at 86°. It may well be that the oxime obtained by them is a mixture of the geometrical isomers.

Hydrogenolysis of the thiophene-derived β-amino acids described above was effected by heating them with Raney nickel in the presence of dilute aqueous ammonia. In this way β-amino-n-enantoic acid (III, R = H) was obtained from β-(2-thienyl)-β-aminopropionic acid (II, R = H); the yield of the crude product amounted to about 80%. β-Amino-n.caproic acid (III, R = CH_3) was obtained in lower yield; the yield of β-amino-n.-pelargonic acid was very small, while attempts to prepare ϑ,ϑ-dimethyl-β-aminopelargonic acid (III, R = = tert-C_4H_9) by hydrogenolysis of β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid (II, R = tert-C_4H_9) failed. The situation did, however, change radically when hydrogenolysis was carried out on the acetyl derivatives of the thiophene-substituted β-amino acids instead of on the free acids themselves. By this method the acetyl derivatives of the corresponding aliphatic β-amino acids were obtained in good yields. From the acetyl derivative of β-(5-ethyl-2-thienyl-β-aminopropionic acid we obtained the acetyl derivative of β-amino-n.-pelargonic acid in a yield of about 78%, while the acetyl derivative of β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid gave the corresponding derivative of ϑ-dimethyl-β-aminopelargonic acid (yield 55%). On heating the latter with hydrochloric acid we obtained, in over 90% yield, the hydrochloride of ϑ-dimethyl-β-aminopelargonic acid, and on neutralizing this with alkali – the free amino acid. In carrying out hydrogenolysis of the amino acids their acetyl derivatives should be used in preference to the free acids, because in this way foaming during the reaction is reduced considerably; in addition, the extraction of the product of hydrogenolysis is made easier since the spent nickel catalyst may be dissolved in acid and the acetyl derivative extracted from the acid solution with a suitable solvent.

EXPERIMENTAL

β-(2-Thienyl)-β-aminopropionic acid (II, R = H). From 46.2 g of 2-thiophenaldehyde, 46.0 g of malonic acid (for preparation see [15]) and 131 g of ammonium acetate there was obtained 31.4 g of crude β-(2-thienyl)-β-aminopropionic acid (yield 41.2%, m. p. 201-203°) and 13.3 g of β-(2-thienyl)acrylic acid (IV, R = H). After one recrystallization from dilute alcohol the amino acid melted at 210-211° with decomposition (in a pre-heated melting point apparatus) (literature, 207-208° [9]).

After crystallization from dilute (1 : 1) hydrochloric acid the hydrochloride of this amino acid melted at 170-171° (decomp.) (literature, m. p. 169-171° [9]).

The p-toluenesulfonyl derivative of the acid was obtained by the action of p-toluenesulfonyl chloride on a solution of the acid in 10% sodium carbonate, followed by acidification of this solution. After two recrystallizations from dilute alcohol the compound melted at 160°.

Found %: N 4.40, 4.60. $C_{14}H_{15}O_4NS_2$. Calculated %: N 4.31.

β-(5-Methyl-2-thienyl)-β-aminopropionic acid (II, R = CH_3). To 32.2 g of 5-methyl-2-thiophenaldehyde was added 30.5 g of malonic acid, 49.0 g of ammonium acetate and 100 ml of 96% alcohol. The mixture was heated under reflux on a boiling water bath for 6 hours. At the end of this period 49.0 g of ammonium acetate and 50 ml of 96% alcohol were added, after which the mixture was heated for another six hours. The crystals which separated after prolonged cooling were filtered off and washed with alcohol and ether. There was obtained 10.45 g of the crude amino acid, m. p. 205-206° (decomp.). The filtrate was combined with the alcohol washings and the solution was reduced under vacuum to a volume of 200 ml. To the residue was added 30.0 g of ammonium acetate. The mixture was heated for 6 hours on a boiling water bath. On cooling no precipitate formed. The alcohol and part of the ammonium acetate were removed in vacuo and 400 ml of water was added to the residue. β-(5-Methyl-2-thienyl)acrylic acid (IV, R = CH_3) separated as an oil which was extracted with ether. The aqueous layer was separated and freed from ether by blowing air through it. The solution was then neutralized with sodium hydroxide to weakly acid reaction to litmus, after which a saturated solution of cupric acetate was added. This precipitated the copper salt of β-(5-methyl-2-thienyl)-β-aminopropionic acid. The dry salt weighed 9.48 g. On decomposing this salt with hydrogen sulfide there was obtained 5.3 g of the free amino acid (II, R = CH_3). The total yield of the amino acid was, thus, 15.7 g (33%). After recrystallization from boiling water the amino acid melted at 208° with decomposition.

Found %: C 51.97, 51.85; H 5.94, 5.89; S 17.02, 16.97. $C_8H_{11}O_2NS$. Calculated %: C 51.87; H 5.99; S 17.31.

The hydrochloride was obtained by dissolving the amino acid in concentrated hydrochloric acid and evaporating the solution. After recrystallization from conc. hydrochloric acid it melted at 209-210° with decomposition.

Found %: C 43.16, 43.30; H 5.32, 5.51; Cl 15.96, 15.70. $C_8H_{12}O_2NClS$. Calculated %: C 43.14; H 5.43; Cl 15.92.*

The acetyl derivative was obtained in the following way. 0.6 g of the amino acid was dissolved in 10 ml of 6% sodium hydroxide solution and to the cooled solution was added 1 ml of acetic anhydride. The mixture was shaken for one hour and was then acidified with hydrochloric acid (Congo red). There separated colorless crystals (0.64 g, m. p. 140-142°). After recrystallization from dilute alcohol the compound was obtained in the form of long needles, m. p. 143-144°.

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* In all hydrochlorides of the amino acids chloride content was determined by the Volhard method.

Found %: C 52.63, 52.70; H 5.79, 5.71; S 14.16, 14.23; N 6.04, 5.97. $C_{10}H_{13}O_3NS$. Calculated %: C 52.85; H 5.76; S 14.10; N 6.16.

β-(5-Methyl-2-thienyl)acrylic acid (IV, R = CH_3). The ether extract obtained in the preparation of β-(5-methyl-2-thienyl)-β-aminopropionic acid (see above) was washed with 10% sodium carbonate solution (two 100 ml portions). The soda extract was acidified with concentrated hydrochloric acid to Congo red. There separated a yellow oil which crystallized rapidly. There was obtained 6.54 g of impure unsaturated acid melting at 156-160°. After two recrystallizations from dilute alcohol the acid melted at 164-165°. Literature, m. p. 165-166° [16].

Found %: C 57.05, 57.06; H 4.88, 4.95; S 18.81, 18.71. $C_8H_8O_2S$. Calculated %: C 57.12; H 4.79; S 19.06.

Acid ammonium (5-methyl-2-thienyl)-methylenemalonate (V). To a mixture of 17.2 g of 5-methyl-2-thiophenaldehyde, 15.8 g of malonic acid and 21.0 g of ammonium acetate was added 125 ml of 96% alcohol. The mixture was heated under reflux for 4 hours on a boiling water bath. On cooling the entire contents crystallized. The crystals were filtered off and washed with alcohol and ether. The dry substance weighed 25.2 g. After two recrystallizations from dilute alcohol yellow leaflets were obtained which melted at 182°.

Found %: C 46.93, 47.18; H 4.77, 4.88; N 6.14, 6.13. $C_9H_{11}O_4NS$. Calculated %: C 47.15; H 4.84; N 6.11.

On addition of sodium hydroxide to the aqueous solution of the compound there evolved ammonia gas. On heating 15.0 g of this acid ammonium salt with 30 g of ammonium acetate in 100 ml of alcohol (for 18 hours on a boiling water bath) there was obtained 2.8 g of β-(5-methyl-2-thienyl)-β-aminopropionic acid, m. p. 208°.

β-(5-Ethyl-2-thienyl)-β-aminopropionic acid (II, R = C_2H_5). A mixture of 33.5 g of 5-ethyl-2-thiophenaldehyde, 27.4 g of malonic acid, and 33.5 g of ammonium acetate in 100 ml of 96% alcohol was heated under reflux for 6 hours on a boiling water bath, after which another 33.5 g of ammonium acetate was added and heating continued for a further 6 hours. On prolonged cooling of the reaction mixture in ice there separated a crystalline precipitate. This was filtered off and washed several times with alcohol (the alcoholic washings being collected separately), followed by washing with ether. The dry amino acid weighed 11.4 g, m. p. 203° (decomp.). The filtrate obtained after separating the amino acid, was heated for 6 hours. On cooling in ice, there separated an additional quantity of the amino acid (3.08 g, m. p. 200-201°). In this way, 14.5 g of the impure amino acid (30.5%) was obtained in all. From the filtrate obtained from the isolation of the amino acid, there was extracted β-(5-ethyl-2-thienyl)acrylic acid (see below). After two recrystallizations from boiling water the amino acid melted, in preheated melting point apparatus, at 203-204° with decomposition.

Found %: C 54.00, 54.10; H 6.45, 6.54; N 6.79, 7.01. $C_9H_{13}O_2NS$. Calculated %: C 54.24; H 6.57; N 7.03.

After recrystallization from dilute (1 : 1) hydrochloric acid the hydrochloride of the amino acid melted at 170-171° with decomposition.

Found %: C 45.67, 45.55; H 5.51, 5.89; Cl 15.01, 14.81. $C_9H_{14}O_2NClS$. Calculated %: C 45.86; H 5.99; Cl 15.05.

The p-toluenesulfonyl derivative melted, after recrystallization from dilute alcohol at 127-128°.

Found %: N 3.99, 4.04. $C_{16}H_{19}O_4NS_2$. Calculated %: N 3.96.

The acetyl derivative was obtained from 5.0 g of the amino acid dissolved in 80 ml of 6% sodium hydroxide solution, and 8.0 ml of acetic anhydride. In all, there was obtained 5.3 g of the acetyl derivative of β-(5-ethyl-2-thienyl)-β-aminopropionic acid, m. p. 128-130°. After recrystallizing the substance from dilute alcohol its melting point was 129-130°.

Found %: C 55.11; H 6.21; S 13.35. $C_{11}H_{15}O_3NS$. Calculated %: C 54.75; H 6.28; S 13.29.

β-(5-Ethyl-2-thienyl)acrylic acid (IV, R = C_2H_5). From the filtrates obtained in the preparation of β-(5-ethyl-2-thienyl)-β-aminopropionic acid (see above), was isolated 11.7 g of an impure unsaturated acid melting at 87-90°. After two recrystallizations of 1.9 g of the impure acid from dilute alcohol there was obtained 0.75 g of a compound melting at 100-101° (literature m. p. 102-103° [16]).

Found %: C 59.33. 59.43; H 5.55, 5.58. $C_9H_{10}O_2S$. Calculated %: C 59.26; H 5.53.

(5-Ethyl-2-thienyl)methylenemalonic acid. A mixture of 26.6 g of 5-ethyl-2-thiophenaldehyde, 23.8 g of malonic acid, 29.4 g of ammonium acetate and 100 ml of 96% alcohol was refluxed for five hours on a boiling water bath. On cooling the reaction mixture crystallized. The acid ammonium salt of acid (VI) which separated was filtered off and washed several times with alcohol and then with ether. There was obtained 26.6 g of a yellow colored substance. After recrystallization from dilute alcohol the salt melted at 168-169°. On addition of caustic soda to a solution of this salt there evolved ammonia. The free acid (VI) was liberated by acidifying an aqueous solution of its ammonium salt with hydrochloric acid. After recrystallization from dilute alcohol the acid had a melting point of 136-137°.

Found %: C 53.28, 53.22; H 4.47, 4.61. $C_{10}H_{10}O_4S$. Calculated %: C 53.08; H 4.45.

Heating the ammonium salt with ammonium acetate in ethyl alcohol resulted in the formation of β-(5-ethyl-2-thienyl)-β-aminopropionic acid, m. p. 200-201°.

2-Tert-butylthiophene was prepared by the method described by Buu-Hoi and co-workers [10]. To a solution of 84 g of thiophene and 111 g of tert-butyl chloride in 1500 ml of anhydrous carbon disulfide was added, with stirring and cooling to 10-12°, 313 g of stannous chloride over a period of one hour. The mixture was stirred at 20° for five hours and was then poured into 5% of ice-cold hydrochloric acid. The carbon disulfide layer was washed with water, sodium carbonate solution, and again with water and was dried over calcium chloride. After removing the carbon disulfide the residue was fractionated (on a 32-plate column). From 84 g of thiophene there was obtained 72 g (51%) of 2-tert-butyl-thiophene, b. p. 161.8-162.8°, n_D^{20} 1.4982 (Literature, b. p. 163-164°, n_D^{20} 1.4987 [17]; b. p. 163.9°, n_D^{20} 1.49788 [18]; b. p. 165°, n_D^{23} 1.5024 [10]).

5-Tert-butyl-2-thiophenaldehyde was obtained by formulating 2-tert-butyl-thiophene [12]. To a mixture of 38 g of N-methylformanilide and 25 ml of phosphorus oxychloride was added dropwise, with stirring, 30 g of 2-tert-butyl-thiophene, the temperature being kept at 35-40° during the addition, after which stirring was continued for another three hours at room temperature. Next day the mixture was poured on 120 g of crushed ice, extracted with ether, the ether extract washed with dilute hydrochloric acid, water, sodium bicarbonate, followed by another washing with water and was finally dried over magnesium sulfate. After removing the solvent the residue was distilled in vacuo. There was obtained 35 g (97%) of an aldehyde boiling at 133° at 23 mm Hg, n_D^{20} 1.5462, n_D^{22} 1.5451, n_D^{26} 1.5436 (Literature, b. p. 135-136° 25 mm, n_D^{25} 1.5428 [11]; b. p. 246° n_D^{22} 1.5495 [10]; b. p. 135-136° 25 mm, n_D^{25} 1.5441 [12]).

High-melting 5-tert-butyl-2-thiophenaldoxime. To a solution of 0.80 g of hydroxylamine hydrochloride and 0.60 g of sodium carbonate in 10 ml of water was added 1.53 g of 5-tert-butyl-2-thiophenaldehyde followed by addition of alcohol (15 ml) until the solution cleared. The solution was then heated for 1 hour on a boiling water bath and after cooling was acidified with dilute hydrochloric acid (to Congo red). To the warmed acid solution was added water until the solution became permanently turbid. On cooling in ice there separated the yellow-colored crystalline oxime together with some oil. After several recrystallizations from dilute alcohol the oxime became colorless and melted at 118-119°. Literature [10] gives a melting point of 86° (method of preparation not described). Since the melting point of our oxime differed from that given in the literature, the compound was analyzed.

Found %: C 59.01, 58.80; H 7.26, 7.13; S 17.02, 17.13. $C_9H_{13}ONS$. Calculated %: C 58.98; H 7.15; S 17.49.

Low-melting 5-tert-butyl-2-thiophenaldoxime. To a solution of 0.72 g of hydroxylamine hydrochloride and 0.61 g of sodium carbonate in 10 ml of water was added 1.25 g of 5-tert-butyl-2-thiophenaldehyde followed by addition of alcohol in an amount necessary to produce a clear solution. The solution was refluxed on a boiling water bath for 1 hour, after which it was allowed to cool somewhat and to the warm solution was added water until permanent turbidity had developed. On cooling there separated an oil which crystallized on prolonged standing in the cold. Yield, 0.75 g, m. p. 72-74°. After two recrystallizations from dilute alcohol the oxime melted at 73-74°.

Found %: C 59.05, 58.57; H 7.45, 7.48; S 17.55, 17.78. $C_9H_{13}ONS$. Calculated %: C 58.98; H 7.15; S 17.49.

β-(5-Tert-butyl-2-thienyl)-β-aminopropionic acid (II, R = tert-C_4H_9). A mixture of 36.3 g of 5-tert.-butyl-2-thiophenaldehyde, 26.5 g of malonic acid 33.5 g of ammonium acetate and 190 ml of 96% alcohol was heated on a boiling water bath for six hours after which another 33.5 g of ammonium acetate was added and heating continued for a further six hours. After prolonged cooling there separated crystals of the amino acid (12.3 g) having a melting point of 193-195°. After recrystallization from water the acid melted at 213° with decomposition.

Found %: C 58.01, 58.03; H 7.59, 7.38; S 14.25, 14.04; N 6.19, 6.01. $C_{11}H_{17}O_2NS$. Calculated %: C 58.12; H 7.54; S 14.11; N 6.16.

The acetyl derivative obtained from 12.3 g of the amino acid dissolved in 250 ml of 10% sodium carbonate solution warmed to 45°, and 25 ml of acetic anhydride. After acidifying the solution there was obtained 10.8 g of the acetyl derivative. After several recrystallizations from dilute methanol and dilute dioxan the compound melted at 105-106°.

Found %: N 4.90, 5.04. $C_{13}H_{19}O_2NS$. Calculated %: N 5.22.

β-(5-Tert-butyl-2-thienyl)-acrylic (IV, R = tert-C_4H_9). The mother liquor obtained after separation of the foregoing aminopropionic acids, was treated as described in the case of the isolation of β-(5-methyl-2-thienyl)acrylic acid. There was obtained 27.1 g of the crude unsaturated acid having yellowish color. After several recrystallizations from dilute alcohol the acid melted at 140°. The pure acid has a pale yellow color.

Found %: C 62.75, 62.81; H 6.67, 6.52; S 15.11, 15.34. $C_{11}H_{14}O_2S$. Calculated %: C 62.82; H 6.71; S 15.24.

β-Amino-n-enantoic acid (III, R = H). To a solution of 10.0 g of β-(2-thienyl)-β-aminopropionic acid in 200 ml of water and 50 ml of a concentrated solution of ammonia was added gradually at a temperature of 70°, with stirring, about 75 g of Raney nickel.* (The spontaneous foaming occurred during the addition.) After stirring at 70-75° for six hours the compound still contained sulfur.** After addition of another 15 g of the catalyst and stirring for a further three hours at 70-75° the reaction for sulfur was negative. The nickel catalyst was then filtered off and washed repeatedly with hot water. The combined filtrates were evaporated under reduced pressure to a volume of about 200 ml. The warm residue was filtered off from the aluminum hydroxide which had separated, and was then evaporated to dryness under reduced pressure on a water bath.

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*Raney nickel was prepared by the standard method [20], but the passing of hydrogen during the washing of the catalyst from alkali was omitted.

**Sulfur was tested for as follows: 2-3 ml of the solution was filtered from the catalyst and evaporated to dryness in a test tube. To the residue was added a small piece of sodium and the test tube was heated to red heat and then plunged into a beaker containing 5-10 ml of water; the resulting solution was filtered. The appearance of a raspberry color on addition of dilute solution of sodium nitroprusside indicated the presence of sulfur.

The impure amino acid weighed 6.7 g (79 %), m. p. 196-198°. After recrystallization from absolute alcohol (with charcoal) the amino acid melted at 201-202°.

Found %: C 57.74, 58.00; H 10.42, 10.53; N 9.52, 9.69. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

The hydrochloride of the amino-enantoic acid was obtained from 2.5 g of the impure acid dissolved in 5 ml of warm concentrated hydrochloric acid. On cooling, crystals of the hydrochloride separated from the solution. After drying in a vacuum dessicator over phosphorus pentoxide the substance weighed 1.34 g. After several recrystallizations from conc. hydrochloric acid the hydrochloride melted at 115-116°.

Found %: C 46.54, 46.43; H 8.78, 8.88; Cl 19.43, 19.41. $C_7H_{16}O_2NCl$. Calculated %: C 46.27; H 8.88; Cl 19.52.

The acetyl derivative was prepared as follows. To a solution of 3.2 g of the amino acid in 80 ml of 6% sodium hydroxide solution, cooled to 0°, was added 6.0 ml of acetic anhydride. After two hours the solution was acidified with hydrochloric acid but no precipitate formed. The solution was then reduced on a water bath to a volume of about 30 ml and was decanted from the salt which separated. On standing in the cold there separated colorless crystals (2.05 g) which after several recrystallizations from hot water melted at 74.5-76°.

Found %: C 57.59, 57.76; H 9.05, 9.20. $C_9H_{17}O_3N$. Calculated %: C 57.73; H 9.14.

The p-toluenesulfonyl derivative of the amino-enantoic acid was obtained by the action of p-toluenesulfonyl chloride on a solution of the amino acid in 10% sodium carbonate solution, followed by acidification of the solution. After recrystallization from dilute alcohol the compound melted at 94-95°.

Found %: C 56.40. 56.22; H 7.00, 7.15; S 10.89, 11.03. $C_{14}H_{21}O_4NS$. Calculated %: C 56.16; H 7.07; S 10.71.

4-n-Butyldehydrouracil. 4.5 g of β-amino-n-enantoic acid, 20.0 g of urea and 50 ml of water were heated on a boiling water bath for 15 hours. The filtered solution was extracted with ether, the aqueous layer was acidified with hydrochloric acid and evaporated to dryness with repeated additions of hydrochloric acid. To the dry residue was added 50 ml of water. The insoluble portion was filtered off and washed with water. The weight of the dry substance was 3.1 g, m. p. 168°. After recrystallization from dilute alcohol the melting point was unaltered.

Found %: C 56.11, 56.15; H 8.26, 8.16; N 16.32, 16.56. $C_8H_{14}O_2N_2$. Calculated %: C 56.45; H 8.29; N 16.46.

β-Amino-n-caprylic acid (III, R = CH_3) was obtained in low yield by hydrogenolysis of β-(5-methyl-2-thienyl)-β-aminopropionic acid carried out as described in the case of the amino-enantoic acid. After recrystallization from alcohol the substance melted at 202-204° (decomp.). Literature [19], m. p. 204-206° (decomp.).

Found %: N 8.48, 8.48. $C_8H_{17}O_2N$. Calculated %: N 8.80.

4-n-Amyldehydrouracil was prepared by heating β-amino-n-caprylic acid with urea followed by evaporation of the solution with hydrochloric acid. After two recrystallizations from dilute alcohol, m. p. 181-182° (literature, m. p. 182-184° [19]).

Found %: C 58.36, 58.55; H 8.64, 8.59; N 15.27, 15.10. $C_9H_{16}O_2N_2$. Calculated %: C 58.65; H 8.76; N 15.22.

β-Amino-n-pelargonic acid (III, R = C_2H_5). Hydrogenolysis of 5.0 g of β-(5-ethyl-2-thienyl)-β-aminopropionic acid yielded only 0.74 g of β-amino-n-pelargonic acid. After recrystallization from hot water the melting point was 205°. Mixture with a specimen of β-amino-pelargonic acid prepared by V. K. Zvorykina [7] melted at 204-205°.

The p-toluenesulfonyl derivative of this amino acid was obtained as an oil which did not crystallize.

4-n-Hexyldehydrouracil was prepared as indicated above by the action of urea on the amino-pelargonic acid. After recrystallization from dilute alcohol the compound melted at 185-186° and did not depress the melting point of an authentic sample prepared from β-amino-n-pelargonic acid by V. K. Zvorykina [7].

The acetyl derivative of β-amino-n-pelargonic acid. To a solution of 9.0 g of the acetyl derivative of β-(5-ethyl-2-thienyl)-β-aminopropionic acid in 200 ml of water and 50 ml of concentrated ammonia solution was added at a temperature of 70°, with stirring, about 45 g of Raney nickel. After stirring for three hours at 70-75° the test for sulfur was negative. The solution was filtered from the nickel catalyst which was subsequently washed several times with hot water. The filtrates were combined and evaporated to dryness under reduced pressure; the residue was dissolved in 50 ml of 6% sodium hydroxide. The resultant solution was filtered from the precipitate of nickel hydroxide, and the filtrate was acidified with hydrochloric acid (Congo red). The crystals which separated were washed with water and dried in a vacuum dessiccator over phosphorus pentoxide and weighed 6.2 g (77.5%), melting at 96-98°. After recrystallization from dilute alcohol substance melted at 99-100.5° and did not depress the melting point in mixture with the acetyl derivative prepared by acetylation of β-amino-n-pelargonic acid.

The acetyl derivative of ϑ,ϑ-dimethyl-β-amino-n-pelargonic acid. To a solution of 6.0 g of the acetyl derivative of β-(5-tert.butyl-2-thienyl)-β-amino propionic acid in 200 ml of water was added at 70°, 50 ml of concentrated ammonia solution and about 30 g of Raney nickel. Stirring was continued for 6 hours at 70-75°. As the test for sulfur was positive, another 6 g (approx.) of nickel was added and stirring was continued at 70-75° until the test for sulfur was negative (5 hrs.). After separating the nickel catalyst the solution was treated as in the foregoing example. The residue weighed 2.32 g, m. p. 106-108°. The spent nickel catalyst was dissolved with dilute (1 : 1) hydrochloric acid, the solution was neutralized with alkali to pH 5 and extracted with ether. After removing the ether there remained 0.6 g of a substance melting at 108-109°. Thus the combined yield of the crude acetyl derivative amounted to 2.92 g (55%). After recrystallization from dilute methanol the compound melted at 111-112°.

Found %: C 64.14, 63.90; H 10.21, 10.29; N 5.81, 5.69. $C_{13}H_{25}O_3N$. Calculated %: C 64.16; H 10.36; N 5.76.

The hydrochloride was obtained as follows. 3.82 g of the acetyl derivative of the dimethylamino-pelargonic acid and 50 ml of dilute (1 : 1) hydrochloric acid was refluxed for 12 hours. On cooling there separated a copious crystalline precipitate. The crystals were filtered off and washed with cold dilute (1 : 1) hydrochloric acid. After drying in a vacuum dessiccator over phosphorus pentachloride, the hydrochloride weighed 3.14 g, m. p. 185-190°. After two recrystallizations from dilute hydrochloric acid it melted at 195-196° (decomp.).

Found %: C 55.28, 55.51; H 9.92, 9.91; Cl 14.85, 15.19. $C_{11}H_{24}O_2NCl$. Calculated %: C 55.56; H 10.17; Cl 14.91.

ϑ,ϑ-Dimethyl-β-amino-pelargonic acid. 2.12 g of the hydrochloride of this amino acid was dissolved in 20 ml of warm water and to the solution was added 0.36 g of sodium hydroxide; the resultant alkaline solution was acidified (litmus) with acetic acid. On cooling the solution there separated the free amino acids. The dried substance weighed 1.60 g (yield 89%), m. p. 185-187°. After repeated recrystallization from boiling water the amino acid melted at 197-198° with decomposition.

Found %: C 65.37; H 11.39; N 7.02, 6.85. $C_{11}H_{23}O_2N$. Calculated %: C 65.63; H 11.51; N 6.96.

SUMMARY

1. A new method of preparation of aliphatic β-amino acids has been outlined.

2. Following the method developed by V. M. Rodionov, the authors have prepared β-(2-thienyl)-β-aminopropionic acid, β-(5-methyl-2-thienyl)-β-aminopropionic acid, β-(5-ethyl-2-thienyl)-β-aminopropionic acid and β-(5-tert-butyl-2-thienyl)-β-aminopropionic acid, starting from the corresponding substituted 2-thiophenaldehydes.

3. By hydrogenolysis of the above thiophene-substituted amino acids the authors have obtained β-amino-n-enantoic, β-amino-n-caprylic and β-amino-n-pelargonic acid.

4. Hydrogenolysis of the acetyl derivatives of β-(5-ethyl-2-thienyl)-β-aminopropionic and β-(5-tert.-butyl-2-thienyl)-β-aminopropionic acids gave, respectively, the acetyl derivatives of β-amino-n-pelargonic and θ,θ-dimethyl-β-amino-n-pelargonic acids.

5. Saponification of the acetyl derivative of θ,θ-dimethyl-β-aminopelargonic acid with hydrochloric acid yielded the hydrochloride of θ,θ-dimethyl-β-aminopropionic acid; neutralization of the latter gave the free amino acid.

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Received December 15, 1956

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF PYRROLIDINE BASES FROM γ -KETOALCOHOLS

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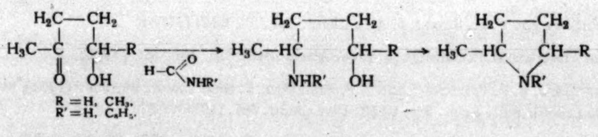
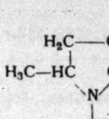
In a preliminary communication we have shown [1] that on heating γ -acetopropyl alcohol and secondary γ -acetobutyl alcohol with formamide and N-phenylformamide in the presence of a nickel catalyst amination and reduction of the carbonyl group takes place, followed by ring closure through the NH_2 and OH groups in positions 1,4. The reaction products were identified as the corresponding pyrrolidine bases, namely, α-methylpyrrolidine (I), 2,5-dimethylpyrrolidine (II), N-phenyl-2-methylpyrrolidine (III) and N-phenyl-2,5-dimethylpyrrolidine (IV).



In the present paper we describe these syntheses in greater detail and we show the possibility of an extension of this reaction.

Continuing our investigation of the hydroamination of γ -acetopropyl and of secondary γ -acetobutyl alcohols we employed different N-substituted derivatives of formamide (N-methylformamide, N-ethylformamide, N-p-tolylformamide, N-o-tolylformamide, N-p-anisylformamide, N-o-anisylformamide). In all cases we obtained the corresponding pyrrolidine bases.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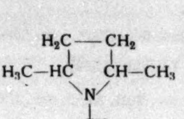
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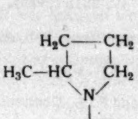
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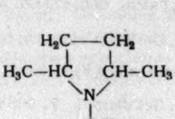
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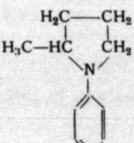
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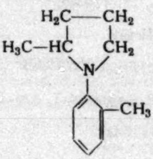
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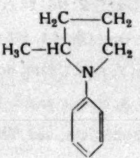
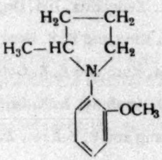

(XI)


(XII)

The necessary N-substituted derivatives of formamide were prepared prior to the hydroamination reaction by mixing the corresponding amine with formic acid (to strongly acid reaction to Congo red), followed by distillation from the mixture of water and excess formic acid up to 160° (thermometer in reaction mixture). The N-substituted formamides contained a small amount of residual formic acid.

In all cases the nickel catalyst was found to facilitate lowering of the reaction temperature without appreciably affecting the yields of the pyrrolidine bases which varied from 20 to 50%. In the case of α-methylpyrrolidine we were able to raise the yield to 30% (cf. our previously published data [1]).

In the case of secondary γ-acetobutyl alcohol the yields of the corresponding pyrrolidine bases were always lower and in general did not exceed 30%. This fact would suggest that the presence of substituents in positions 2,5, on the one hand, hinders ring closure, while on the other it renders such a ring unstable under the given reaction conditions. This suggestion finds confirmation in some investigations of transformations of heterocyclic compounds carried out by Iu. K. Iur'ev [2].

EXPERIMENTAL

γ-Acetopropyl alcohol. The material used was technical acetopropyl alcohol (commercial) distilled twice in vacuo.

B. p. 114-115° (30 mm) n_D^{20} 1.4395, d_4^{20} 1.0068, MR_D 26.69. Literature data for acetopropyl alcohol [3]: b. p. 115-116 (30 mm) n_D^{20} 1.4390.

Secondary γ-acetobutyl alcohol was prepared by condensing the sodium derivative of acetoacetic ester with propylene oxide [4]. The condensation was effected without isolating α-aceto-γ-valerolactone whereby it was possible to raise the yield of secondary γ-acetobutyl alcohol to 72%.

B. p. 60-61° (4 mm) n_D^{20} 1.4328, d_4^{20} 0.9634, MR_D 31.31; calc. 31.44. Literature [4]: b. p. 79-82° (16 mm) n_D^{20} 1.4312, d_4^{25} 0.9626.

α-Methylpyrrolidine (I). A mixture of 30.6 g of freshly distilled acetopropyl alcohol, 90 g of formamide and 3 g of nickel catalyst (prepared by ignition of nickel formate) was heated at 110-120° until the evolution of carbon dioxide ceased (10-14 hours). As the evolution of the gas subsided the temperature was gradually raised to 160° (thermometer dipping in the reaction mixture). The reaction product was hydrolyzed by refluxing with 150 ml of concentrated hydrochloric acid for 2-3 hours. After cooling, the reaction mixture was transferred into a three-necked flask provided with a stirrer, reflux condenser and dropping funnel, and was mixed with 50 ml of ether. To the well-stirred and cooled mixture was added, slowly and dropwise, a 40% solution of caustic soda to strongly alkaline reaction. The ether layer was then separated, the aqueous layer was extracted several times with ether, and the combined ether extracts were dried with fused alkali. After removing the ether and distilling the residue twice there was obtained 7.5 g (30%) of α-methylpyrrolidine.

B. p. 97-98.5° at 744 mm; n_D^{20} 1.4340, d_4^{20} 0.8343, MR_D 26.58; calc. 26.69. Literature [5]: b. p. 104-104.5° at 755 mm, n_D^{20} 1.4372, d_4^{20} 0.8307.

The picrate of α-methylpyrrolidine was formed in anhydrous ether, m. p. 88.5-89.50°.

1,2-Dimethylpyrrolidine (V). A mixture of 20.4 g of acetopropyl alcohol, 60 g of methylformamide and 2 g of Ni (from nickel formate) was heated at 110-160° until evolution of carbon dioxide ceased. Hydrolysis was effected by refluxing with 100 ml of concentrated hydrochloric acid. The subsequent treatment was similar to that described above for α-methylpyrrolidine. 5.6 g (28%) of 1,2-dimethylpyrrolidine was obtained.

B. p. 92-94° (747 mm) n_D^{20} 1.4240, d_4^{20} 0.7983, MR_D 31.70; calc. 31.64. Literature [5]: b. p. 96-97° (752 mm) n_D^{20} 1.4252, d_4^{20} 0.7994.

The picrate was formed in alcohol, m. p. 235-236°.

Found %: C 44.03, 44.25; H 4.98, 5.20. $C_{12}H_{16}O_7N_4$. Calculated %: C 43.90; H 4.91.

1,2,5-Trimethylpyrrolidine (VI). Thirteen g of sec-γ-acetobutyl alcohol, 45 g of freshly distilled methylformamide and 1.5 g of Ni was heated at 110-160° until carbon dioxide ceased to evolve. After hydrolysis by refluxing with 60 ml of concentrated hydrochloric acid, 1,2,5-trimethylpyrrolidine was isolated as described in the foregoing preparations. There was obtained 2.5 g (20%) of 1,2,5-trimethylpyrrolidine.

B. p. 111-112°(732 mm) n_D^{20} 1.4260, d_4^{20} 0.7987, MR_D 36.32; calc. 3626. Literature [6]: b. p. 115-116° (750 mm) d_4^{20} 0.8149.

The picrate was formed in alcohol, m. p. 162-164° (decomp.).

Found %: C 45.78, 45.79; H 5.63, 5.33. $C_{13}H_{18}O_7N_4$. Calculated %: C 45.61; H 5.30.

1-Ethyl-2-methylpyrrolidine (VII). On heating 20.4 g of acetopropyl alcohol, 60 g of freshly distilled ethylformamide and 2 g of nickel catalyst, and treating the reaction mixture as described above, there was obtained 11.3 g (50%) of 1-ethyl-2-methylpyrrolidine.

B. p. 117.5-118°(752 mm) n_D^{20} 1.4300, d_4^{20} 0.8052, MR_D 36.31; calc. 36.26. Literature [5]: b. p. 119-120° (754 mm) n_D^{20} 1.4325, d_4^{20} 0.8028.

The picrate was formed in alcohol, m. p. 192-193°.

Found %: C 45.80, 45.70; H 5.49, 5.42. $C_{13}H_{18}O_7N_4$. Calculated %: C 45.61, H 5.30.

1-Ethyl-2,5-dimethylpyrrolidine (VIII). Heating a mixture of 15 g of sec-γ -acetobutyl alcohol, 45 g of freshly distilled ethylformamide and 1.5 g of Ni, followed by the usual treatment, yielded 3.2 g (20.8%) of 1-ethyl-2,5-dimethylpyrrolidine.

B. p. 132-134° (746 mm) n_D^{20} 1.4290, d_4^{20} 0.80524, MR_D 40.66; calc. 40.88. Literature [7]: b. p. 130-131.5°.

The picrate was formed in alcohol, m. p. 192-193°.

Found %: C 46.57, 46.93; H 5.77, 5.61. $C_{14}H_{20}O_7N_4$. Calculated %: C 47.29; H 5.65.

1-p-Tolyl-2-methylpyrrolidine (IX). A mixture of 30.6 g of γ -acetopropyl alcohol, 96 g of freshly distilled formyl-p-toluidine and 3 g of Ni was heated at 110-115° until evolution of carbon dioxide ceased. The reaction mixture (dark viscous liquid, solidifying on cooling) was hydrolyzed by refluxing with 75 ml of concentrated hydrochloric acid for 3 hours. After cooling 40% sodium hydroxide solution was added to the contents of the flask to strongly alkaline reaction. The dark oily layer which separated was removed, the aqueous layer extracted with ether, and the combined extracts were dried with fused alkali. After removing the ether the residue was distilled in vacuo. Excess p-toluidine came over first, followed by 1-p-tolyl-2-methyl pyrrolidine. After two distillations and treatment with benzenesulfonyl chloride there was obtained 31 g (59%) of 1-p-tolyl-2-methylpyrrolodine.

B. p. 133-134° (10 mm) n_D^{20} 1.5580, d_4^{20} 0.9664, MR_D 58.45; calc. 55.76. Literature [2]: b. p. 115° (5 mm) n_D^{20} 1.5572, d_4^{20} 0.9648, MR_D 58.12.

The picrate (formed in alcohol) melts at 128-131°.

Found %: C 53.35, 53.50; H 5.15, 5.13. $C_{18}H_{20}O_7N_4$. Calculated %: C 53.46; H 4.99. Literature [2]: b. p. 115° (5 mm) n_D^{20} 1.5572, d_4^{20} 0.9648; MR_D 58.12.

1-o-Tolyl-2-methylpyrrolidine (X). Heating a mixture of 20.4 g of acetopropyl alcohol, 54 g of formyl-o-toluidine and 1.5 g of Ni, followed by the treatment described for compound (IX), gave 8.3 g (23%) of 1-o-tolyl-2-methylpyrrolidine.

B. p. 100-102°(8 mm) n_D^{20} 1.5405, d_4^{20} 0.9693, MR_D 56.77; calc. 55.75. Literature [2]: b. p. 97-98° (5 mm) n_D^{20} 1.5438, d_4^{20} 0.9725, MR_D 56.79.

The picrate melts at 145-146° (from alcohol).

Found %: C 53.59, 53.69; H 5.07, 5.29. $C_{18}H_{20}O_7N_4$. Calculated %: C 53.46; H 4.99.

1-p-Anisyl-2-methylpyrrolidine (XI). Interaction of 20.4 g of γ-acetopropyl alcohol with 80 g of formyl-p-anisidine in the presence of 1.5 g of Ni, followed by treatment similar to that described above, yielded 11.5 g (40%) of 1-p-anisyl-2-methylpyrrolidine.

B. p. 160°(12 mm) n_D^{20} 1.5625, d_4^{20} 1.0480, MR_D 59.21; calc. 57.40.

The picrate melts at 161-162° (from benzene).

Found %: C 51.99, 51.88; H 4.99, 4.90. $C_{18}H_{20}O_8N_4$. Calculated %: C 51.42; H 4.79.

1-o-Anisyl-2-methylpyrrolidine (XII). Heating 30.6 g of γ-acetopropyl alcohol, 80 g of formyl-o-anisidine and 3 g of Ni gave 19 g (33%) of 1-o-anisyl-2-methylpyrrolidine.

B. p. 127-129°(10 mm) n_D^{20} 1.5570, d_4^{20} 1.0428; MR_D 58.90; calc. 57.40.

The picrate melts at 162-163.5°.

Found %: C 54.18, 54.14; H 5.40, 5.35. $C_{18}H_{20}O_8N_4$. Calculated %: C 51.42; H 4.79.

SUMMARY

1. Hydroamination of γ-acetopropyl and sec-γ-acetobutyl alcohols with formamide and its N-substituted derivatives has been investigated. It has been shown that the reaction gives rise to the formation of the corresponding pyrrolidine bases in yields of 20-50%.

2. The lower yield of pyrrolidine bases obtained from sec-γ-acetobutyl alcohol appears to be due to the instability of the pyrrolidine ring having substituents in positions 2,5.

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Received December 30, 1956

HALOARYLATION OF UNSATURATED COMPOUNDS BY AROMATIC DIAZO COMPOUNDS

X. SYNTHESIS OF DL-PHENYLALANINE AND ITS HOMOLOGS

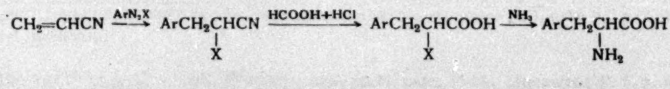
A. M. Iurkevich, A. V. Dombrovskii, and A. P. Terent'ev

L-Phenylalanine belongs to the number of the so-called essential amino acids. D-Phenylalanine enters into the composition of the antibiotic gramicidin C. Some of the derivatives of phenylalanine are of significance as biologically active materials. Thus, 3-methyltyrosine, p-fluorophenylalanine, and 2,5-dimethylphenylalanine show a specific inhibiting effect on decarboxylase and in connection with this they lower the blood pressure [1]. p-Nitrophenylalanine is a structural element of the antibiotic Chloromycetin.

In this connection the search for new methods of synthesis of phenylalanine and its derivatives that differ from those described in the literature in their greater simplicity and the availability of the starting materials is of much significance.

Gaudry [2] succeeded in preparing phenylalanine (I) and tyrosine (II), which were contaminated with cinnamic and p-hydroxycinnamic acids, from α-chloro-β-arylpropionitriles in small yields (17-20 %). The reason for the small yields of (I) and (II) was the unfortunate choice of a method of hydrolysis of the chloropropionitriles with concentrated sulfuric or hydrochloric acid. L'Eckyer [3] showed by the example of the hydrolysis of methyl-α-chloro-β-(p-nitrophenyl)isobutyrate that under these conditions splitting out of hydrogen chloride and formation of α-methyl-p-nitrocinnamic acid occurs simultaneously with the hydrolysis of the ester. M. M. Shemiakin and coworkers [4] described the synthesis of (I) and (II) labeled with N^{15} from the corresponding esters of α-bromo-β-phenyl- and α-bromo-β-(p-methoxyphenyl)propionic acids and potassium N^{15} phthalimide. In turn, the ester of bromophenylpropionic acid was prepared from natural phenylalanine. Therefore this method cannot serve for the preparation of phenylalanine derivatives. Moreover, as has been shown in one of our reports [5], of cinnamic acids and phthalimide are formed in high yields by the action of potassium phthalimide on esters of α-halo-β-arylpropionic acids.

Employing the haloarylation of derivatives of acrylic acid [6], we have developed a method [7] for the synthesis of α-halo-β-arylpropionic and β-arylbutyric acids by hydrolysis of the nitriles and esters of these acids with a mixture of formic and hydrochloric acids. This permitted us further to find a general method of synthesis of DL-β-phenylalanine and its derivatives from acrylonitrile and methylmethacrylate.



$$CH_2{=}CHCN \xrightarrow{ArN_2X} ArCH_2\underset{X}{\underset{|}{C}}HCN \xrightarrow{HCOOH+HCl} ArCH_2\underset{X}{\underset{|}{C}}HCOOH \xrightarrow{NH_3} ArCH_2\underset{NH_2}{\underset{|}{C}}HCOOH$$

As a rule aminonitriles are not produced by the direct action of ammonia and amines on α-halo-β-arylpropionitriles. An exception is α-chloro-β-phenylpropionitrile (III), which upon treatment with aniline and subsequent hydrolysis of the aminonitrile by heating with potassium hydroxide yields N,β-diphenylalanine. By heating (III) and α-chloro-β-(p-nitrophenyl)propionitrile (IV) with urotropine in dioxane and subsequent decomposition of the urotropine complex with an alcoholic solution of HCl, the hydrochlorides of the ethyl esters of phenylalanine and p-nitrophenylalanine (V) were obtained in satisfactory yields.

In search of a convenient method for the preparation of amino acids we subjected α-halo-β-arylpropionic acids to amination by one of three methods: by the action of a concentrated aqueous solution of ammonia, by the action of liquid ammonia, and finally, by the action of urotropine. As a result we obtained 50-90% yields of phenylalanine (I), p-methoxyphenylalanine (VI), p-chlorophenylalanine (VII), 2,4-dichlorophenylalanine (VIII), and p-bromophenylalanine (IX). From (VI) we prepared tyrosine (II) in 90% yield. In the synthesis of the acids mentioned, the use of liquid ammonia always gave higher yields than working in aqueous solutions. In addition, the reaction proceeded more rapidly.

Attempts to prepare (V) by direct amination of α-chloro-β-(p-nitrophenyl)propionic acid (X) proved unsuccessful, since in this case p-nitrocinnamic acid always was formed. Amination of (X) with urotropine permitted us to obtain (V) in good yield.

Recently a synthesis has been described for a homolog of (I) – α-methyl-β-phenylalanine (XI) – carried out by a very complex method [8] in 5-6 stages, starting with benzyl cyanide. We prepared (XI) and α-methyl-β-(p-nitrophenyl)alanine, and also their esters, by amination with urotropine of the corresponding α-chloro-β-arylisobutyric acids, for which a means of synthesis has previously been proposed by us [7].

EXPERIMENTAL

Phenylalanine (I) from α-chloro-β-phenylpropionic acid (XII). a) Action of aqueous ammonia solution. 1.5 g of (XII) was heated in a sealed ampoule with 5 ml of 25% ammonia solution and 2 g of ammonium carbonate at 40-50° for 60 hours. After cooling, the ampoule was opened and the contents after 10 hours boiling were evaporated on a water bath to a volume of 1 ml. The solid residue was separated, washed with ice water, and dried. 0.5 g (40%) of phenylalanine was obtained. M. p. 271-272° (with decomp.) after recrystallization from water. By treatment of 0.35 g of (I) with benzoyl chloride (1 ml) in solution at 0°, we obtained N-benzoyl-β-phenylalanine with m. p. 186-187°. A melting point test of a mixture of this product and N-benzoyl-β-phenylalanine from phenylalanine prepared from acetamidomalonic ester and benzoyl chloride [9] gave no depression.

b) Action of liquid ammonia. One g of (XII), 0.5 g of ammonium chloride, and 50 ml of liquid ammonia were placed in an ampoule. After the mixture had stood for 3 days at 20° and had been worked up in the usual manner, 0.37 g of phenylalanine (42%) was obtained with m. p. 272-273° (with decomp.).

Phenylalanine (I) from α-bromo-β-phenylpropionic acid (XIII). a) Action of aqueous ammonia solution. In a bottle with a ground glass stopper were placed 27 g of (XIII) and 250 ml of concentrated ammonia solution, and the mixture was shaken on a rocking device for 7 days at 18-20°. After the usual treatment, 14.5 g of phenylalanine (74%) was obtained with m. p. 271-273° (with decomp.).

b) Action of liquid ammonia. From 2 g of (XIII), 1 g of ammonium chloride, and 50 ml of liquid ammonia at 20° (3 days) we obtained 1.15 g of phenylalanine (80%) with m. p. 273° (with decomp.).

p-Methoxyphenylalanine (VI) from α-chloro-β-(p-methoxyphenyl)propionic acid. From 1.7 g of (XIV), 1 g of ammonium chloride, and 50 ml of liquid ammonia (20°, 3 days) we obtained in the usual way 1.1 g of (VI) with m. p. 291-293° (with decomp.). Yield 70%. Literature data: m. p. 293° (with decomp.) [10].

p-Methoxyphenylalanine from α-bromo-β-(p-methoxyphenyl)propionitrile (XV). 4.4 g of (XV) was heated in a flask with a reflux condenser to 100° with 10 ml of 85% formic acid and 10 ml of concentrated hydrochloric acid. The mixture was diluted with water and the oil that separated was removed, dried, and shaken with 50 ml of concentrated ammonia solution (6 days at 20°). After the usual treatment, we obtained 1.7 g of (VI). Yield 45%. After recrystallization from aqueous alcohol, a white, crystalline compound was obtained that melted at 292° (with decomp.).

Tyrosine (II) from p-methoxyphenylalanine (VI). 1.7 g of (VI) was dissolved in 15 ml of acetic anhydride and 1.5 g of red phosphorus and 15 ml of hydriodic acid were added. After heating for 4 hours, cooling, and neutralization, 1.4 g of (II) was obtained. Yield 90%. After reprecipitation from alkali solution, a white, fluffy powder was obtained with m. p. 298° (with decomp.). Literature data: m. p. 298-299°; 311-313° (with decomp.) [11].

p-Chlorophenylalanine (VII). From 3 g of α-chloro-β-(p-chlorophenyl)propionic acid (XVI) and 100 ml of aqueous ammonia (7 days at 20° on a shaker) we obtained 0.77 g of (VII) with m. p. 239° (with decomp.). Yield 30%.

From 3 g of (XVI), 1 g of ammonium chloride, and 50 ml of liquid ammonia we obtained 2.15 g of (VII) with m. p. 238-239° (with decomp.). Yield 83%. Literature data: m. p. 236-241° [9], 253° [12].

p-Bromophenylalanine (IX). From 5 g of α-chloro-β-(p-bromophenyl)propionic acid, 3 g of ammonium chloride, and 100 ml of liquid ammonia (20°, 3 days) we obtained 3.94 g of (IX) as colorless plates with m. p. 254-255° (with decomp.). Yield 85%. Literature data: m. p. 258° (with decomp.) [13].

2,4-Dichlorophenylalanine (VIII). From 4.2 g of α-chloro-β-(2,4-dichlorophenyl)propionic acid, 3 g of ammonium chloride, and 100 ml of liquid ammonia we obtained 3.5 g of (VIII) with m. p. 237-239° (with decomp.) as needle-like crystals. Yield 96%. Literature data: m. p. 238-240° (with decomp.) [14].

p-Nitrophenylalanine (V). Five g of (X) was dissolved in 50 ml of dioxane and boiled with 18 g of urotropine for 4 hours. After cooling the precipitate was filtered off and washed with chloroform to remove the urotropine, then treated with an alcoholic solution of HCl, diluted with water, and boiled for 2 hours. After treatment with ammonia and evaporation, 3.28 g of (V) was obtained with m. p. 240-245° (with decomp.); the preparation darkened at 215-220°. Yield 72%. Literature data: m. p. 240-245° (with decomp.) [15].

Hydrochloride of the ethyl ester of phenylalanine from α-chloro-β-phenylpropionitrile (III). From 12 g of (III) and 30 g of urotropine in 100 ml of dioxane (boiling for 3 hours) we obtained by a method similar to that described above 4.95 g (30%) of the hydrochloride of the ethyl ester of phenylalanine with m. p. 126-127° (rosy-white plates). Literature data: m. p. 127° [16].

Hydrochloride of the ethyl ester of p-nitrophenylalanine from α-chloro-β-(p-nitrophenyl)propionitrile (IV). From 10 g of (IV) and 30 g of urotropine in 100 ml of dioxane (boiling for 3 hours) we obtained 5.2 g (40%) of the hydrochloride of the ethyl ester of p-nitrophenylalanine as lemon-yellow crystals with m. p. 177-180°. Literature data: m. p. 179-180° [13].

α-Methyl-β-phenylalanine (XI). From 15 g of α-chloro-β-phenylisobutyric acid and 35 g of urotropine in 200 ml of dioxane we obtained by the usual method (refluxing for 3 hours) 10.6 g (65%) of the hydrochloride (XI) with m. p. 236° (with decomp.). Literature data: m. p. 241-143° [8].

α-Methyl-β-(p-nitrophenyl)alanine (XVII). From 11 g of α-chloro-β-(p-nitrophenyl)isobutyric acid and 30 g of urotropine in 200 ml of dioxane (boiling for 3 hours) we obtained 8.2 g (70%) of the hydrochloride (XVII) with m. p. 273-274°. Literature data: m. p. 275-277° [8].

N,β-Diphenylalanine (XVIII) from aniline and α-chloro-β-phenylpropionitrile (III). In a flask with a reflux condenser we heated 5 g of (III) and 9.8 g of aniline on an oil bath at 130-140° for 8 hours. After cooling, the mixture was treated with 50 ml of water, and the oil was separated and subjected to hydrolysis with alcoholic potassium hydroxide (2 g of KOH per 25 ml of alcohol and 10 ml of water), the excess aniline was steam distilled off, and the contents of the flask were quickly filtered, cooled, and acidified with concentrated sulfuric acid; 2.8 g of (XVIII) was obtained as a white, crystalline powder with m. p. 172-173°. Yield 41%. Literature data: m. p. 173° [17].

SUMMARY

1. A method has been developed for the synthesis of β-aryl-α-amino acids by the amination of α-halo-β-arylpropionic and α-halo-β-arylisobutyric acids with concentrated aqueous ammonia solution, liquid ammonia, and urotropine.

2. The conversion of α-halo-β-arylpropionitriles to amino acids has been investigated.

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Moscow State University Received November 26, 1956

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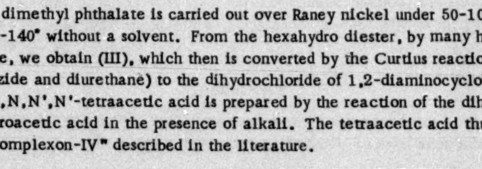
SUBSTANCES CAPABLE OF FORMING COMPLEXES

I. SYNTHESIS AND STRUCTURE OF "COMPLEXON-IV" — 1,2-DIAMINOCYCLOHEXANE-N,N,N',N'-TETRAACETIC ACID

V. G. Iashunskii and M. N. Shchukina

According to patent data [1], "Complexon-IV"— 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (I) — the most effective of the presently known complexons [2] — is obtained by the condensation of 1,2-diaminocyclohexane (II) with chloroacetic acid or with formaldehyde and sodium cyanide. In addition, it is pointed out [1] that the diamine is synthesized starting with anthranilic acid by the method of Einhorn [3] by reduction with metallic sodium in alcohol and subsequent conversion to the ester, amide, and (by the Hofmann reaction) diamine. Both this and other methods of preparation described in the literature for (II) [4-6] are not very suitable for producing (I) in adequate amounts.

We have developed a convenient method for preparing 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid starting with the available dimethyl (or diethyl) phthalate; in this we have utilized data from the work of Wieland et al., [4], who synthesized (II) from the dihydrazide of cyclohexanedicarboxylic-1,2 acid (III) by the Curtius reaction. By our method (I) is obtained in four stages according to the following diagram:



Hydrogenation of dimethyl phthalate is carried out over Raney nickel under 50-100 atm. pressure and at a temperature of 110-140° without a solvent. From the hexahydro diester, by many hours' boiling with excess hydrazine hydrate, we obtain (III), which then is converted by the Curtius reaction (without isolation of the intermediate diazide and diurethane) to the dihydrochloride of 1,2-diaminocyclohexane (II). 1,2-Diaminocyclohexane-N,N,N',N'-tetraacetic acid is prepared by the reaction of the dihydrochloride of the diamine with monochloroacetic acid in the presence of alkali. The tetraacetic acid thus synthesized has all the properties of the "Complexon-IV" described in the literature.

On the basis of the high complex-forming ability of (I) Schwarzenbach [7] suggested that the nitrogen atoms in this compound have a cis-configuration with respect to the cyclohexane ring; Prishibil [2] also pointed out that the existence of trans-derivatives of (I) was unknown up to that time. However, there is no experimental evidence supporting the cis-configuration (I). For the cyclohexane ring, which can assume a "bed" form and a "chair" form, the spatial arrangement of the two neighboring substituents in the cis- and trans-isomers can differ little from one another; therefore, the a priori assumption that just the cis-configuration of "Complexon-IV" is required by its high complex-forming ability is, in our opinion, not entirely justified. For the purpose of clarifying the configuration of (I), we carried out a proof of the structure of the 1,2-

diaminocyclohexane that we prepared. Jaeger [5] showed that 1,2-diaminocyclohexane synthesized by the reduction of the dioxime of cyclohexanedione-1,2 with sodium in alcohol had the trans-structure; however, he actually did not describe derivatives of this amine. We repeated the work of Jaeger and the diamines obtained by the two methods (from the dioxime and from the dihydrazide) gave identical derivatives, corresponding in their properties to the derivatives of 1,2-diaminocyclohexane synthesized by Einhorn [3]. Consequently, the 1,2-diaminocyclohexane prepared by us and that from which (I) was prepared according to the patent data had the trans-configuration. From this it follows that "Complexon-IV" also is trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid.

Comparison of the magnitudes of the apparent dissociation constants and the stability constant of the Ca-complex (CaX^{-2}) of the tetraacetic acid obtained by us (determined by the potentiometric method) with those given in the work of Schwarzenbach [7] for the corresponding values for (I) again shows conclusively that the two tetraacetic acids are identical and that "Complexon-IV" has the trans-configuration (see Table 1).

TABLE 1

	Inverse logarithms of apparent dissociation constants*				Stability constant of the complex CaX^{-2}, where X is the tetra-acid group, K_{Ca}*
	pK_1	pK_2	pK_3	pK_4	
"Complexon-IV" [7]	2.4	3.5	6.12	11.70	$10^{12.5}$
Trans-diaminocyclohexane-N,N,N',N'-tetraacetic acid	2.7**	3.6**	6.15	11.70	$10^{12.5}$

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*In 0.1 M KCl solution at 20°.

** The difference in values is connected with the lesser resolving power of our potentiometer.

EXPERIMENTAL

Dimethyl ester of cyclohexane-1,2-dicarboxylic acid. By the hydrogenation of 262 g of dimethyl phthalate over 6 g of nickel catalyst in an autoclave with a volume of 2 l at 110-140° and an initial pressure of 80-100 atm (1.5÷2 hours) we obtained 256 g (95%) of dimethyl ester of cyclohexane-1,2-dicarboxylic acid with b. p. 140° at 26 mm; n_D^{20} 1.4618.

Dihydrazide of cyclohexane-1,2-dicarboxylic acid (III). One-hundred g of the hexahydro diester was added over the course of 8 hours to 75 g of 100% hydrazine hydrate, which was heated to boiling in a 1-liter round-bottomed flask connected with a reflux condenser and dropping funnel. The mixture was heated at 130-135° (temperature of oil bath) for 24 hours more and the solid white mass that formed was dissolved in 1 liter of boiling water. The crystals that precipitated on cooling were separated with suction, washed with cold water and alcohol, and dried in an oven at 110°. From the mother liquor it was possible to isolate some additional quantity of the dihydrazide. In all we obtained 73-74.5 g of dihydrazide with m. p. 227-230°, which amounted to a yield of 73-74.5% calculated on the hexahydro diester. After recrystallization from water and drying, m. p. 229-231°.

Found %: C 47.86; H 8.09; N 27.75. $C_8H_{16}O_2N_4$. Calculated %: C 48.00; H 8.05; N 27.98.

Dihydrochloride of trans-1,2-diaminocyclohexane (II). Fifty g of the dihydrazide (III) was added to 170 ml of 10% hydrochloric acid in a three-necked flask, fitted with a mechanical stirrer, thermometer, and dropping funnel, while the contents were cooled (16-20°), and in the course of 20-25 minutes a solution of 34.5 g of sodium nitrite in 75 ml of water was introduced, while the temperature of the mixture was kept

TABLE 2

Titration of Tetra-Acid with 0.1 M KOH at 20°, $\mu = 0.1$

	In the absence of $Ca^{\cdot\cdot}$						In the presence of $Ca^{\cdot\cdot}$ ($CaCl_2$); $C_{Ca} = 0.01$		
$C_T^a \cdot 10^{-4}$	1.000	1.320	1.427	3.454	3.560	3.772	3.880	2.540	2.755	2.955
	9.97	9.95	9.94	9.76	9.75	9.73	9.72	9.80	9.78	9.76
$[H^{\cdot}]$	$3.16 \cdot 10^{-4}$	$1.86 \cdot 10^{-4}$	$1.48 \cdot 10^{-4}$	$3.16 \cdot 10^{-11}$	$2.34 \cdot 10^{-11}$	$1.51 \cdot 10^{-11}$	$1.26 \cdot 10^{-11}$	$1.48 \cdot 10^{-4}$	$1.32 \cdot 10^{-4}$	$1.10 \cdot 10^{-4}$

Notes: a) number of moles of KOH consumed per mole of tetra-acid, C_T – concentration of tetra-acid. $pK_1 = 2.7$; $pK_2 = 3.6$; $pK_3 = 6.15$; $pK_4 = 11.70$; $pK_3' \times pK_4 = 7.3$; $\log K_{Ca} = 12.5$; $K_{Ca} = 10^{12.5}$.

within the limits 18-20°. After a brief period of stirring, the aqueous solution was extracted with 400 ml of methylene chloride. 250 ml of anhydrous ethyl alcohol was added to the dried extract, and after the methylene chloride was distilled off (below 75°) the mixture was refluxed for 2 hours. After this, 350 ml of 40% sodium hydroxide solution was added and the mixture was steam-distilled in a flask with a drip trap. In 4-5 hours the distillation was completed and the distillate was acidified with hydrochloric acid. After evaporation to dryness, 26-29 g of the dihydrochloride of 1,2-diaminocyclohexane was obtained, which could be recrystallized from dilute hydrochloric acid. M. p. 232-326° (decomp.).

Found %: Cl 37.78; N 14.90. $C_6H_{14}N_2 \cdot 2HCl$. Calculated %: Cl 37.91; N 14.97.

By reduction of the dioxime of cyclohexane-1,2-dione with metallic sodium in ethyl alcohol [4] we obtained the dihydrochloride of trans-1,2-diaminocyclohexane (yield 51%) with m. p. 322-325° (from 10% HCl).

Both samples of the diamine dihydrochloride gave identical derivatives: a) diacetyl derivative with m. p. 263-264° (from a mixture of ethyl acetate and ethyl alcohol);

b) dibenzoyl derivative with m. p. 340-343° (from glacial acetic acid).

Found %: C 74.22; H 6.91. $C_{20}H_{22}O_2N_2$. Calculated %: C 74.50; H 6.88.

c) dibenzene sulfonyl derivative with m. p. 153-155° (from 40% ethyl alcohol).

Trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid. Seventy-eight ml of 25% solution of sodium hydroxide (chem. pure) was added, with external cooling, to 59 g of monochloroacetic acid, and then 23.35 g of diamine dihydrochloride (II) was introduced. While the mixture was stirred and heated on a boiling water bath, 25% sodium hydroxide solution was added at such a rate that a sample continuously colored thymolphthalein paper blue. In 10-15 minutes about 80 ml of the alkali was used, i.e., the principal amount. Heating and stirring of the mixture was continued for 3 hours more, during which time another 15-20 ml of alkali was added. The hot solution was acidified with concentrated hydrochloric acid (17-20 ml) and treated with activated carbon, and by further addition of concentrated hydrochloric acid (about 25 ml to a pH of 1.5-2) the tetraacetic acid was precipitated; this was then washed with distilled water and dried at 60-70°. 24.4 g of the monohydrate of trans-1,2-diaminocyclohexanetetraacetic acid was obtained (53.5% calculated on the dihydrochloride, which could be recrystallized from a large amount of water for complete purification.

Found %: C 46.20; H 6.56; H_2O 4.86. $C_{14}H_{22}O_8N_2 \cdot H_2O$. Calculated %: C 46.15; H 6.64; H_2O 4.94.

Upon heating to 100° under reduced pressure the monohydrate split out a molecule of water.

Potentiometric determination and calculation of the dissociation constant were carried out by the method of Schwarzenbach [8], employing the data of Martell and Calvin [9]. A LP-5 potentiometer was used for the work. By way of example, the results of one of the parallel titrations are presented (see Table 2).

SUMMARY

1. A convenient method has been developed for the preparation of trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid.

2. It has been shown that the "Complexon-IV" described in the literature has the trans-configuration.

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Received December 19, 1956

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METHYL LINOLEATE MONOXIDE AND ITS PROPERTIES

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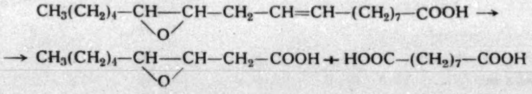
In 1929 a report was published by one of us with A. Ia. Vasil'ev [1, 2] on the preparation of a dioxide of methyl linoleate (m. p. 32.1°) and a liquid isomer of it. On saponification of the crystalline isomer a dioxide of linoleic acid (m. p. 76.4°) was isolated. In the same year articles by Böeseken et al., appeared [3, 4], in which the authors obtained the same results. The question of the possibility of obtaining an unsaturated monoxide of linoleic acid remained open. It was found, however, that the oxidation of methyl linoleate by benzoyl hydrogen peroxide goes stepwise: first one double bond is oxidized, the second double bond being oxidized considerably more slowly. It is also known that hydrogenation [5] and bromination [6] of linoleic acid proceed in two phases. The multiple bonds of linoleic acid, consequently, have a different reactivity. All this provided a basis for us to assume that the synthesis of a monoxide of linoleic acid could be accomplished.

To carry this out, the methyl ester of linoleic acid was oxidized with acetyl hydrogen peroxide prepared (to avoid contamination with acetyl peroxide) from boroacetic anhydride. The monoxide of methyl linoleate was a colorless oil with b. p. 173-175° (0.08 mm).

The structure of the monoxide was demonstrated on the basis of its oxidation by potassium permanganate in acetone solution. If the oxygen ring was on the 12 and 13 carbon atoms, we should find the oxide of nonenoic acid and azelaic acid among the oxidation products.



$$CH_3(CH_2)_4-\underbrace{CH-CH}_{O}-CH_2-CH{=}CH-(CH_2)_7-COOH \rightarrow$$
$$\rightarrow CH_3(CH_2)_4-\underbrace{CH-CH}_{O}-CH_2-COOH + HOOC-(CH_2)_7-COOH$$

But if the oxygen ring was formed with the 9 and 10 carbon atoms, then the oxidation products should be caproic acid $C_6H_{12}O_2$, and the oxide of dodecenoic acid.

As a result of the oxidative decomposition of the monoxide of linoleic acid we isolated azelaic acid and the oxide of nonenoic acid (m. p. 56-57°), from which we obtained the barium salt. In addition, acetic and, apparently, caproic acids were found among the oxidation products that were volatile with steam. The two latter acids could be produced only as a result of breakdown of the oxide of nonenoic acid, since the oxide of dodecenoic acid was not found in the oxidation products.

However, we did not wish to be limited by these data. To clarify the structure of the monoxide of linoleic acid it was necessary to obtain the hydrogenated monoxide of this acid. If the hydrogenated oxide had the structure of the oxide of 6-octadecene-18-carboxylic acid, its properties should be different from those of the oxide of oleic acid (i.e., the oxide of 9-octadecene-18-carboxylic acid).

Actually an oily liquid with b. p. 190.5-191.0° (0.7 mm) was obtained by the hydrogenation of the monoxide of methyl linoleate. By saponification of this product an oxide was produced (m. p. 18.5-19.6°) that differed in its properties from the oxide of oleic acid. On reaction with ammonia [7] it gave a hydroxyaminostearic acid with m. p. 84-85°. *

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* The hydroxyaminostearic acid prepared from the oxide of oleic acid melted at 154-155°.

The monoxide of methyl linoleate had unusual properties that were dependent on the proximity of the oxygen ring to the double bond. In our first experiments on catalytic hydrogenation of the unsaturated monoxide obtained by us, a high reactivity was observed for the double bond. Having encountered this phenomenon, we carried out a comparative hydrogenation of methyl linoleate and the methyl ester of the oxide of linoleic acid. As can be seen from the figure, addition of the hydrogen necessary to saturate one double bond proceeded at the same rate for both compounds. Thus, the results of hydrogenation showed that the double bond in the linoleic acid monoxide molecule has the same activity, as the most reactive double bond (Δ^{12}) of linoleic acid.

EXPERIMENTAL

Preparation of methyl linoleate. The starting material for the synthesis of linoleic acid was linoleic acid tetrabromide obtained directly from the mixed acids of sunflower oil. The tetrabromide was characterized by its m. p. 114.5°. Yield 47%. The linoleic acid was synthesized from the tetrabromide by treatment of the latter with zinc in pyridine solution by the method of Kaufmann.

It was found experimentally that the best weight ratio of zinc, tetrabromide, and pyridine was 1 : 1 : 2. The zinc was used in the form of thin flakes, purified of zinc oxide.

The linoleic acid synthesized in this way was esterified in the presence of methyl alcohol saturated with hydrogen chloride. The methyl linoleate boiled at 196-197° (8 mm). The yield based on the bromide employed was 45.2%.

Found: iodine number 172.05, 171.50. $C_{19}H_{34}O_2$. Calculated: iodine number 172.79.

Synthesis of the monoxide of methyl linoleate. Acetyl hydrogen peroxide was made from boroacetic anhydride. To a solution of 58 g of methyl linoleate in 300 ml of ether was added 200 ml of an ethereal solution of acetyl hydrogen peroxide (containing 3.31 g of active oxygen). Spontaneous heating of the reaction mixture was not observed. The reaction was completed in 45 hours. On fractional distillation of the oxidized methyl linoleate a fraction was isolated with b. p. 195-197° (6 mm).

d_4^{20} 0.9376, n_D^{20} 1.4600. MR_D 90.56. calc. 90.57.

Found %: C 72.78, 72.93; H 11.21, 11.06; iodine number 81.1, 81.6; ester number 181.10, 183.14. $C_{19}H_{34}O_3$. Calculated %: C 73.48; H 11.06; iodine number 81.93; ester number 180.97.

Monoxide of linoleic acid. The monoxide of methyl linoleate was saponified and the free monoxide of linoleic acid was separated from the saponification products by the usual methods as a yellowish oil that solidified on cooling to fine crystals (m. p. 18-19°). Soluble in methyl alcohol and in ethyl and petroleum ethers.

Oxidation of the monoxide of linoleic acid with potassium permanganate.

To 150 ml of acetone was added 1.8 g of $NaHCO_3$. 8.7 g of linoleic acid monoxide was added to the suspension that was obtained, and then powdered potassium permanganate was added in small portions, with cooling with ice water and continuous shaking, until decoloration ceased. In all 40.5 g of $KMnO_4$ was added. Then the acetone was removed from the reaction mixture by distillation. The residue was washed 5 times with 5% KOH solution. The combined wash waters were concentrated to 200 ml and acidified with sulfuric acid. The acid solution was extracted with ethyl ether. The residue obtained after removal of the ether from the solution was treated with steam. In the distillation flask, upon cooling, a white precipitate separated out, which was dissolved in an excess of hot water. A layer of oil that came to the surface on cooling was extracted with ether. From the aqueous solution that had been concentrated to 50 ml a crystalline precipitate separated on cooling with ice. After recrystallization from water it melted at 105.8°. A mixed sample with azelaic acid did not give a depression in melting point.

Found: neutralization equivalent 303.96, 304.70. $C_9H_{16}O_4$. Calculated: neutralization equivalent 304.58.

The ether was removed from the ethereal solution that was obtained by treatment of the contents of the distillation flask. The residue, which consisted of an oil and crystals, was washed with water to remove traces of azelaic acid. The dried product melted at 56-57°.

Found: neutralization equivalent 341.0, 324.6. $C_9H_{16}O_3$. Calculated: neutralization equivalent 326.0.

After neutralization with ammonia and addition of $BaCl_2$, the barium salt of the oxide of nonenoic acid precipitated.

Found %: Ba 28.31, 28.9. $(C_9H_{15}O_3)_2Ba$. Calculated %: Ba 28.64.

From the distillate obtained on treatment of the oxidation product with steam a mixture of two acids was extracted, one of which seemed readily soluble in water, and the other in alcohol. Barium salts were obtained from both acids.

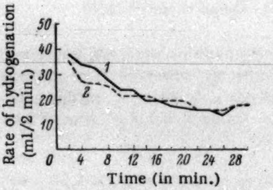
Ba salt of acid soluble in water.

Found %: Ba 52.52. $(C_2H_3O_2)_2Ba$. Calculated %: Ba 53.2.

Ba salt of acid soluble in alcohol.

Found %: Ba 35.24. $(C_6H_{11}O_2)_2Ba$. Calculated %: Ba 37.2.

Catalytic hydrogenation of the monoxide of methyl linoleate. 2.2359 g of the monoxide, 10 ml of ethyl alcohol, and 0.103 g of catalyst (PtO_2) were shaken in an atmosphere of hydrogen. The total volume of hydrogen absorbed was 311 ml at 18° and 774 mm (calculated 306 ml). The volume of hydrogen absorbed for each 2 minutes (rate of hydrogenation) was: 34, 27, 25, 26, 21, 21, 21, 19, 19, 20, 15, 17, 13, 16, 17 ml (see Figure).



Graph of comparative catalytic hydrogenation of methyl linoleate and methyl ester of linoleic acid monoxide. 1) Methyl linoleate, 2) methyl ester of linoleic acid monoxide.

The hydrogenation product, after removal of the alcohol and traces of methyl stearate (m. p. 37°) that were formed, was distilled twice in vacuo. By distillation a fraction was obtained with b. p. 190.5-191° (7 mm) that was a clear liquid with a slight odor.

d_4^{20} 0.9319, n_D^{20} 1.45307, MR_D 90.58; calc. 91.03.

Found %: C 72.62, 72.45; H 11.45, 11.68; ester number 180.38, 180.44. $C_{19}H_{36}O_3$. Calculated %: C 73.03; H 11.61; ester number 179.5.

Addition of ammonia to the oxide of 6-octadecene-18-carboxylic acid. 0.98 g of the oxide and 10 ml of concentrated ammonia solution were placed in a thick-walled ampoule. The sealed ampoule was heated in a thermostat at 120° for 10 hours. Then the contents of the ampoule, a clear liquid, were poured into a porcelain dish and allowed to stand for two days. As the ammonia evaporated, a white cloud began to appear. The remaining ammonia was removed in a vacuum desiccator. A slightly yellowish mass readily soluble in alcohol, remained in the dish. From the alcohol solution crystals of hydroxyaminostearic acid with m. p. 84-85° precipitated on cooling.

SUMMARY

The monoxide of methyl linoleate had the structure of the methyl ester of 12,13-oxido-9-octadecene-1-carboxylic acid. By hydrogenation of this compound the oxide of the methyl ester of 6-octadecene-18-carboxylic acid was formed.

It has been made clear that the double bond of the methyl ester of 12,13-oxido-9-octadecene-1-carboxylic acid is hydrogenated at the same rate as the double bond of Δ^{12}-methyl linoleate.

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Received January 9, 1957

INVESTIGATION OF AROMATIC COMPOUNDS WITH A LONG SIDE CHAIN

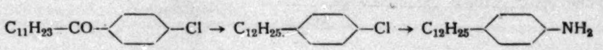
II. PREPARATION OF DODECYLANILINE BY AMMONOLYSIS OF p-CHLORODODECYLBENZENE

L. N. Nikolenko and K. K. Bablevskii

It is known that homologs of aniline can be prepared by the reduction of the corresponding nitro compounds [1]; however, there are no data in the literature on the preparation of p-n-dodecylaniline by this method. There are directions in the literature for the preparation of p-dodecylaniline in small yields by the catalytic isomerization of N-dodecylaniline at temperatures below 240° in the presence of $ZnCl_2$ and $CoCl_2$ [2, 3]. The isomerization is accompanied by a large amount of by-products.

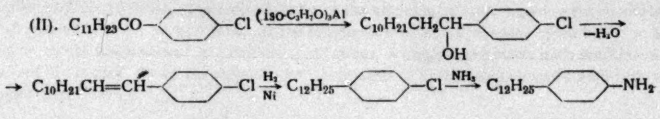
In our previous communication [4] it was shown that p-n-dodecylaniline, like a number of other homologs of aniline containing a normal aliphatic chain in the para position to the amino group, can be obtained by the reduction of alkyl (4-aminophenyl) ketones with amalgamated zinc and hydrochloric acid. In the present work we describe the preparation of p-n-dodecylaniline by the replacement of chlorine by the amino group in p-chlorododecylbenzene, which in turn was prepared from p-chlorolaurophenone by two different methods, namely by the reduction in one stage of p-chlorolaurophenone by a modified Kishner method [5] and by a poly-stage method: first p-chlorolaurophenone was reduced with aluminum isopropylate to dodecyl-(4-chlorophenyl)carbinol, the carbinol was further dehydrated in vacuo over potassium bisulfate heated to 200°, and finally the p-chlorododecenylbenzene obtained was hydrogenated on a Raney nickel catalyst.

(I).



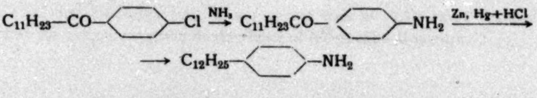
In spite of the many-stage procedure, the yield of p-chlorododecylbenzene by the second method was higher (75%) than by the reduction of p-chlorolaurophenone by the Kishner method (65.7%). The p-chlorododecylbenzene was further converted to p-dodecylaniline by heating it for 6 hours with 30% aqueous ammonia solution to 250° in the presence of cuprous chloride.

(II).



In comparing the methods for the preparation of dodecylaniline, it should be pointed out that the yield based on the starting p-laurophenone by Scheme I was 54.5%, and that by Scheme II was 60%, while it did not exceed 47.5% when the compound was prepared through undecyl (4-aminophenyl) ketone (Scheme III).

(III).



By direct alkylation of aniline with alcohols in the presence of $ZnCl_2$ [3], p-dodecylaniline was obtained as the main reaction product with a yield up to 32%.

EXPERIMENTAL

Preparation of undecyl-(4-chlorophenyl)carbinol [6]. 29.5 g of p-chlorolaurophenone and 100 ml of 1 M aluminum isopropylate solution were heated on a water bath in a flask with a Gan* dephlegmator until there was a negative reaction in the distillate for acetone (test with 2,4-dinitrophenylhydrazine). After most of the isopropyl alcohol was distilled off in vacuo and the reaction mixture was cooled, the residue was treated with dilute hydrochloric acid (1 : 2) and the undecyl-(4-chlorophenyl)carbinol was extracted with benzene. After the solvent was distilled off from the solution, which had been dried with sodium sulfate, the product was distilled in vacuo. 27.9 g (94%) of undecyl-(4-chlorophenyl)carbinol was obtained with b. p. 207.5° (at 5 mm), freezing point 22.5°, n_D^{25} 1.5042.

Found %: C 72.96, 72.83; H 9.99, 9.86; OH 5.70, 5.67. $C_{18}H_{29}OCl$. Calculated %: C 72.83; H 9.85; OH 5.73.

Preparation of p-chlorododecenylbenzene. To 8.2 g of fused, finely pulverized potassium bisulfate, heated to 200° at a residual pressure of 10 mm, was added dropwise 16.5 g of undecyl-(4-chlorophenyl)carbinol. When addition of the carbinol was finished, the mixture was heated at the indicated temperature for another 20 minutes and the product was then distilled at a bath temperature of 230°. 13.5 g (86.5%) of p-chlorododecenylbenzene was obtained. On repeated distillation a product was obtained with b. p. 214° (at 10 mm), freezing point 25°, $n_D^{25.5}$ 1.5200.

Found %: C 77.83, 77.68; H 9.86, 9.95. $C_{18}H_{27}Cl$. Calculated %: C 77.54; H 9.76.

Preparation of p-chlorododecylbenzene by reduction of p-chlorododecenylbenzene. 27.9 g of p-chlorododecenylbenzene in 70 ml of anhydrous alcohol was reduced at atmospheric pressure on 1.5 g of Raney Ni. 2240 ml of hydrogen was absorbed in 7 hours. After removal of the nickel, the catalyzate was diluted with an equal amount of water, and the oily layer was separated, dried with calcium chloride, and distilled. 25.5 g (91.2%) of p-chlorododecylbenzene was obtained with b. p. 196.5° (at 5 mm), freezing point 9.5°, n_D^{20} 1.4920, d_4^{20} 0.9361.

Found %: C 77.33, 77.20; H 10.51, 10.39. $C_{18}H_{29}Cl$. Calculated %: C 76.96; H 10.41.

Reduction of p-chlorolaurophenone by a modification of the Kishner method. A mixture of 12 g of p-chlorolaurophenone, 52 ml of diethylene glycol, 5.2 g of sodium hydroxide, and 20 ml of hydrazine hydrate was heated on a boiling water bath with vigorous stirring for 24 hours. Then the temperature was slowly raised to 185° and the hydrazine hydrate partially distilled off. The mixture was kept at this temperature for 8 hours. On completion of the reduction, the mass was poured into water and the p-chlorododecylbenzene was extracted with ether. After the ether was distilled off, the product was distilled in vacuo. 7.5 g (65.7%) of p-chlorododecylbenzene was obtained with b. p. 213.5° (at 15-17 mm), freezing point 9.5°, n_D^{20} 1.4925.

Found %: C 77.10, 76.88; H 10.53, 10.49. $C_{18}H_{29}Cl$. Calculated %: C 76.96; H 10.41.

Preparation of p-dodecylaniline. 10.7 g of p-chlorododecylbenzene, 1.2 g of copper chloride, and 300 ml of 30% ammonia solution were heated at 250° in an autoclave for 6 hours. After extraction from the reaction mass with ether, the dodecylaniline was isolated as the hydrochloride by passing a current of dry hydrogen chloride through the ethereal solution. 8.6 g (80.2%) of dodecylaniline hydrochloride was obtained. To isolate the free amine, the hydrochloride was treated with 10% sodium hydroxide solution. A product was obtained with m. p. 40.5-41°. A mixed sample with dodecylaniline prepared by the reduction of p-aminolaurophenone (m. p. 41.5-42°) gave no depression in melting point.

SUMMARY

1. p-Chlorolaurophenone has been reduced to dodecyl-(4-chlorophenyl)-carbinol, by the dehydration

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* Transliteration of Russian—Publisher's note.

of which p-chlorododecenylbenzene was obtained; by hydrogenation of the latter on Raney Ni p-chlorododecylbenzene was obtained.

p-Chlorododecylbenzene also was obtained by direct reduction of p-chlorolaurophenone by a modified Kishner method.

2. It has been shown that p-n-dodecylaniline can be prepared in up to 80% yield by the amination of p-chlorododecylbenzene.

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Received December 14, 1956

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*Original Russian pagination. See C. B. Translation.

**In Russian.

β-ACYLOXYACROLEINS

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Up until the present time β-acyloxyacroleins have remained unknown compounds of the general formula AcOCH=CH—CH=O (I) containing the reactive system of an α,β-unsaturated aldehyde and offering interest as starting materials for a number of syntheses.

We have prepared these compounds by the reaction of the sodium salt of malonic dialdehyde (II) with acid chlorides. When acetyl, propionyl, n-butyryl, or benzoyl chloride was used, satisfactory results were obtained by "method A"— treatment of the acid chloride with a suspension of the sodium salt of malonic dialdehyde in an inert solvent (see experimental section). The starting salt (II) was prepared by us by hydrolyzing 1,1,3,3-tetraethoxypropane [1] in the presence of traces of hydrochloric acid and subsequently neutralizing with sodium hydroxide solution. The reactions with p-nitrobenzoyl chloride or chlorocarbonic ester were carried considerably more conveniently by "method B," by the action of the acid halide on an aqueous solution of salt (II).

β-Acyloxyacroleins that contain an aliphatic acid group are liquids which have an acrid, characteristic odor, are distillable in vacuo, and show an exaltation of the molecular refraction; the compounds with an aromatic acyl group are crystalline substances. All the β-acyloxyacroleins are soluble in the usual organic solvents except petroleum ether; they are insoluble in water and in aqueous solutions of sodium carbonate, but are rapidly hydrolyzed by them with the formation of malonic dialdehyde. The compounds (I) do not give an immediate color reaction with ferric chloride solution; the coloration that appears later is the result of hydrolysis. They give typical reactions for the aldehyde group; in the presence of an excess of semicarbazide they form only monosemicarbazones (which are converted by heating with sodium acetate solution to the amide of pyrazole-1-carboxylic acid). They are easily condensed with salts of guanidine, forming 2-aminopyrimidine.

All of the properties that have been enumerated confirm the structures (I) for the compounds that have been prepared, and are not in keeping with the structure of the acylmalonic dialdehydes $AcCH(CH=O)_2$, the formation of which might be be expected if the acylation reaction proceeded with a shift in the reaction center.

The properties and analytical data for the β-acyloxyacroleins (I) that were prepared and for their semicarbazones are given in Tables 1 and 2.

EXPERIMENTAL

Preparation of the sodium salt of malonic dialdehyde (II). A mixture of 22 g of 1,1,3,3-tetraethoxypropane, 8 ml of 1 N HCl solution, and 20 ml of water was stirred at 50-55° until it was homogeneous. After 10 minutes' standing at room temperature, the solution was titrated slowly with 5 N NaOH solution until it was alkaline to phenolphthalein. The solution obtained was evaporated in vacuo almost to dryness (bath temperature 40-50°), and the residue was treated with a mixture of anhydrous alcohol and acetone (1:3). 8.6 g of the dihydrate of the sodium salt of malonic dialdehyde was obtained; from the mother liquor another 0.7 g of less pure material was obtained after dilution with acetone. Total yield 71%. The compound was dried to constant weight in vacuo at 60°. For analysis, the salt was dissolved in water, precipitated with acetone, and dried in vacuo.

TABLE 1

β-Acyloxyacroleins of the General Formula AcOCH=CH–CH=O

Ac	Method	Yield (% calc. on acyl halide)	B. p. or m. p.	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Analysis (%) found**** C	Analysis (%) found**** H	Analysis (%) calculated C	Analysis (%) calculated H
CH_3CO	A	59	57.5—59° (at 4 mm)	1.1204	1.4703	28.27	26.49	52.37	5.52	52.68	5.25
C_2H_5CO	A	53	49—50 (at 1.5 mm)	1.0 07	1.4710	33.10	31.10	56.04	6.37	56.25	6.25
n-C_3H_7CO	A	42	67—68 (at 2.5 mm)	1.0451	1.4676	37.77	35.72	59.04	7.15	59.15	7.04
C_6H_5CO	A	80	63*	—	—	—	—	68.10	4.66	68.18	4.57
	B	47									
p-$O_2NC_6H_4CO$	B	54**	130—131***	—	—	—	—	54.52	3.30	54.30	3.17
CH_3OCO	B	55	50—50.5*	—	—	—	—	46.34	4.66	46.15	4.61

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*From a mixture of ether and petroleum ether.

**Found %: N 6.23, 6.06. Calculated %: N 6.33.

***From dioxane.

****Average values from two determinations are given.

Found %: Na 23.89, 24.33. $C_3H_3O_2Na$. Calculated %: Na 24.45.

Preparation of β-acetoxyacrolein (method A). 1.6 g of acetyl chloride was added gradually, with stirring, to a suspension of 2.8 g of anhydrous sodium salt of malonic dialdehyde in 20 ml of anhydrous ether; the mixture was stirred at room temperature for 10 minutes more and filtered; hydroquinone was added to the filtrate, the ether was evaporated in vacuo, and the residue was distilled. 1.35 g (59% calculated on acetyl chloride) of β-acetoxyacrolein was obtained with b. p. 57.5-59° at 4 mm (Table 1).

Preparation of β-acetoxyacrolein semicarbazone. To a solution of 0.4 g of β-acetoxyacrolein in 2 ml of alcohol was added an aqueous solution of 0.4 g of semicarbazide hydrochloride and 0.54 g of sodium acetate. 0.41 g of semicarbazone was obtained with m. p. 172-173° (with decomp., from aqueous alcohol) (Table 2). A similar experiment was carried out using a triple excess of semicarbazide hydrochloride (1.2 g). As a result 0.5 g of monosemicarbazone was obtained with m. p. 172-173° (with decomp., from aqueous alcohol).

Preparation of β-(p-nitrobenzoxy)-acrolein (method B). 6.6 g of 1,1,3,3-tetraethoxypropane was hydrolyzed (method A). To the aqueous solution of salt (II) obtained after neutralization was added 30 ml of chloroform, after which a solution of 4.32 g of p-nitrobenzoyl chloride in 40 ml of chloroform was added dropwise, very slowly. The chloroform layer was washed with a sodium bicarbonate solution, then with water, and dried. The residue after evaporation of the chloroform was recrystallized from ethyl acetate. Yield of β-(p-nitrobenzoxy)acrolein 2.7 g (53% calculated on acid chloride), m. p. 129-130°. After recrystallization from dioxane, m. p. 130-131°.

Amide of pyrazole-1-carboxylic acid. A mixture of 0.4 g of β-butyroxyacrolein semicarbazone, 16 ml of 50% alcohol, and 0.26 g of crystalline sodium acetate was heated for a half hour on a boiling water bath. After the solution had cooled 0.02 g (36%) of the amide of pyrazole-1-carboxylic

TABLE 2

Semicarbazones of β-Acyloxyacroleins of the General Formula $AcOCH{=}CH{-}CH{=}N{-}NHCONH_2$

Ac	Melting point	Analysis (%)					
		found *			calculated		
		C	H	N	C	H	N
CH_3CO	172—173° (with decomp., from aq. alc.)	42.39	5.29	24.59	42.10	5.26	24.56
C_2H_5CO	154—155 (with decomp., from aq. alc.)	45.53	5.94	22.40	45.40	5.94	22.69
n.-C_3H_7CO . . .	150—151 (with decomp., from aq. alc.)	48.31	6.66	21.55	48.24	6.53	21.10
C_6H_5CO	171 (with decomp. from methanol)	56.63	4.79	18.17	56.65	4.72	18.01
p-$O_2NC_6H_4CO$ . .	173—174 (with decomp., from dioxane)	47.63	3.79	19.80	47.48	3.59	20.14
CH_3OCO	169—170 (with decomp., from aq. alc.)	38.81	4.85	22.40	38.50	4.81	22.46

acid was obtained, which did not give any depression in melting point when mixed with a sample obtained by another method [2].

2-Aminopyrimidine. 0.8 g of β-butyroxyacrolein was added dropwise, with shaking, to a solution of 0.56 g of guanidine hydrochloride in 3 ml of 18% hydrochloric acid solution. After 3 hours an excess of 40% sodium hydroxide solution was added, the thick mass was dried in a desiccator and extracted with hot benzene. 0.27 g (51%) of 2-aminopyrimidine was obtained with m. p. 124-125°, which did not show any depression in melting point when mixed with a sample prepared by another method [2].

SUMMARY

By the reaction of the sodium salt of malonic dialdehyde with acyl halides, a number of β-acyloxyacroleins were prepared which had the general formula

$$AcOCH{=}CH{-}CH{=}O,$$

where Ac is an organic acid group. The properties of this new type of compound were studied.

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Received December 28, 1956

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*Original Russian pagination. See C. B. Translation.

AUTO-OXIDATION OF A METHYLENE GROUP BOUND TO AN AROMATIC NUCLEUS

II. AUTO-OXIDATION OF THE METHYL ESTER OF 9-PHENYLUNDECANOIC ACID

P. G. Sergeev* and A. M. Sladkov

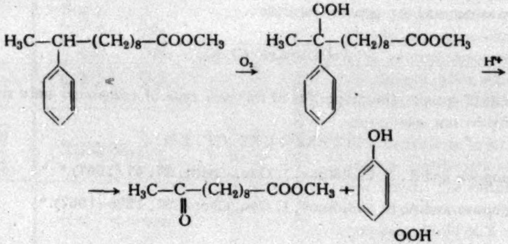
It has been shown by us earlier [1] that the auto-oxidation of compounds, in which the methylene group being subjected to the action of oxygen is simultaneously activated by a phenyl and a carbomethoxy group, proceeds at a fairly rapid rate and in the case of the simpler compounds of this type—the esters of phenylacetic acid—leads to obtaining the esters of phenylglyoxylic acid in high yields.

We became interested in the possibility of auto-oxidizing those types of compounds in which both a phenyl group and an ester group would be present at the same time, but at a sufficient distance from each other to avoid mutual influence on the group being oxidized. We prepared the methyl ester of 9-phenylundecanoic acid as being a suitable compound for studying the indicated reaction. This compound has in its molecule two active centers: the CH group, found in the α-position to the phenyl nucleus, and the CH_2 group, found in the α-position to the carbomethoxy group. The distance of nine carbon atoms between these two activating groups is apparently sufficient to exclude their mutual effect.

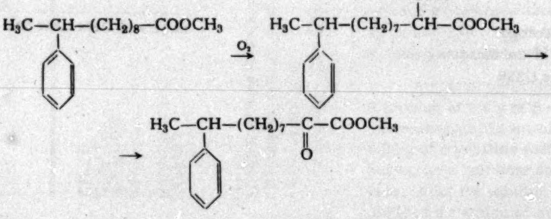
The primary products formed during the reaction, namely hydroperoxides, were converted into simpler products, which made their isolation and identification easier.

The possible directions of the auto-oxidation reaction and the transformations of the first formed hydroperoxides are shown below by the schemes.

I.



II.



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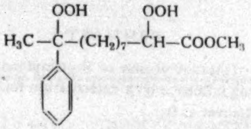
In addition to these two variations for the auto-oxidation reaction and the approximately equal activating influence of the phenyl and carbomethoxy groups, it would also be possible to obtain as a primary reaction product the bis-hydroperoxide with the structure



This hydroperoxide would also be converted into the final product: the methyl ester of 1,9-dioxoundecanoic acid.

Investigation revealed that the auto-oxidation proceeds according to Scheme I, and here a tertiary hydroperoxide is obtained, decomposing under the influence of acids into phenol and the methyl ester of 9-oxoundecanoic acid. Other oxidation products or products of their transformation were not found. This suggests that the activating influence of the phenyl group is much greater than the activating influence exerted by the ester group.

EXPERIMENTAL

Preparation of methyl ester of 9-phenylundecanoic acid. To a suspension of 43 g of anhydrous aluminum chloride in 180 ml of benzene was added 50 g of methyl undecenoate with vigorous stirring. The temperature during reaction was not permitted to rise above 25°. After all of the ester had been added the mixture was stirred for 1.5 hours (total reaction time was 3 hours). The reaction products were poured into water; the oil was separated, washed with water, 5% aqueous potash solution, again with water, and dried over anhydrous sodium sulfate.

We obtained 48.5 g (67%) of methyl 9-phenylundecanoate with b. p. 196-198° at 6 mm.

Found: ester number 135.2 mg/g. $C_{18}H_{28}O_2$. Calculated: ester number 132.7 mg/g.

Auto-oxidation of methyl 9-phenylundecanoate. The process was run in a glass column having a diameter of 12 mm, filled to 2/3 of its height with a packing of cut glass tubes 5 × 2 mm in size. Air was passed at a rate of 0.5 liter/min. through 45 g of the methyl 9-phenylundecanoate at 100°. About 0.01 g of the sodium salt of cumene hydroperoxide was added to initiate the process. After 35 hours the reaction mass contained 11.2% of the hydroperoxide (calculated as the monohydroperoxide; iodometric determination). After 36 hours the hydroperoxide content dropped to 10.8%, for which reason the oxidation was terminated.

Treatment of the reaction mass. An attempt to isolate the formed hydroperoxide from the reaction mass as the sodium salt proved unsuccessful; consequently we decided to decompose the hydroperoxide without isolating it from the reaction mass. For this the oxidation products were diluted with an equal amount of benzene, and then with cooling to 5° and vigorous stirring a drop of concentrated sulfuric acid was added. The reaction mass was stirred and allowed to gradually warm up to room temperature, after which it was heated at 50-60° until a test sample gave a negative test for hydroperoxide. After this the mixture was made exactly neutral by the addition of sodium bicarbonate. Then the benzene was distilled at reduced pressure from the reaction products, and the residue was vacuum-fractionated. The following fractions were isolated: 1st fraction, b. p. 62-64° at 5 mm, 1.8 g; 2nd fraction, b. p. 144-148° at 5 mm, 1.9 g; 3rd fraction, b. p. 194-197° at 5 mm, 40.8 g.

The 1st fraction crystallized completely in the receiver and had m. p. 42°. Its mixture with a specimen of pure phenol did not depress the melting point.

The 2nd fraction was hydrolyzed with a 10% aqueous alcohol solution of sodium hydroxide. Acidification of the hydrolysis products gave an oil, which gradually crystallized. After recrystallization from petroleum ether, m. p. 58-58.5°; literature [2]: 9-oxoundecanoic acid, m. p. 59.5°.

The oxime with m. p. 69-70° (from alcohol) was obtained from the acid; literature [3]: m. p. 68-69°.

Found %: N 5.89. $C_{12}H_{23}O_3N$. Calculated %: N 6.10.

The 3rd fraction was unoxidized methyl 9-phenylundecanoate. It gave a negative test for the carbonyl group.

SUMMARY

1. Based on the auto-oxidation of the methyl ester of 9-phenylundecanoic acid it was shown that the phenyl group exerts a much greater activating influence on a carbon atom found alpha to it, than does the carbomethoxy group on a carbon atom adjacent to it.

2. The scheme for the auto-oxidation of the methyl ester of 9-phenylundecanoic acid was shown, and the decomposition products of the initially formed hydroperoxide were isolated.

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Received December 8, 1956

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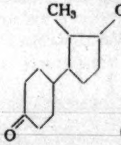
*Original Russian pagination. See C. B. Translation.

ANALOGS OF STEROID HORMONES

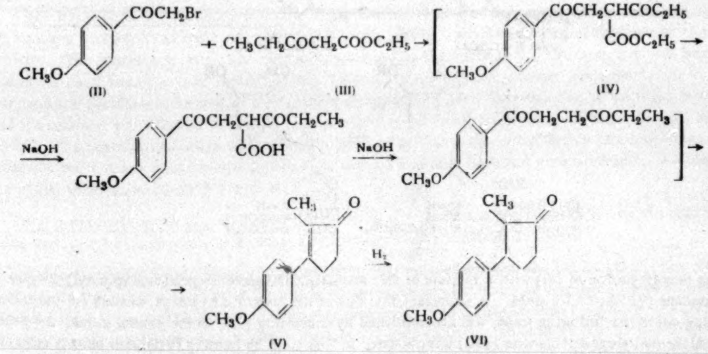
I. PREPARATION OF 3-(4-OXOCYCLOHEXYL)-2-METHYLCYCLOPENTANOL

V. I. Maksimov and Z. A. Priakhina

In this paper we describe the synthesis of 3-(4-oxocyclohexyl)-2-methylcyclopentanol (I), needed by us for the preparation of analogs of steroid hormones not containing the ring C. We started with p-methoxy-ω-bromoacetophenone (II) and ethyl propionylacetate (III), which were converted to 3-(p-methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V) by the reactions based on the method for the preparation of phenylcyclopentanone-containing structures, developed by Borsche [1, 2] and by Weidlich and co-workers [3].



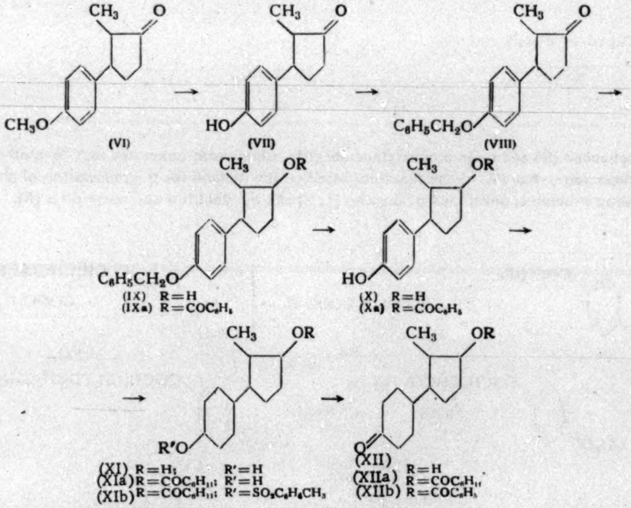
(I)


COCH₂Br
CH₃O
(II)
+ CH₃CH₂COCH₂COOC₂H₅ →
(III)
COCH₂CHCOC₂H₅
COOC₂H₅ →
CH₃O
(IV)
NaOH
COCH₂CHCOCH₂CH₃
COOH
CH₃O
NaOH
COCH₂CH₂COCH₂CH₃
CH₃O
→
CH₃
O
→
CH₃O
(V)
H₂
CH₃
O
CH₃O
(VI)

The sodio derivative of (III) was reacted with (II) in ether medium; the ethyl p-methoxyphenacylpropionylacetate (IV) without being isolated pure was subjected to saponification and ketonic cleavage by heating with 2% aqueous hydroxide solution. The resulting p-methoxyphenyl-1,4-hexanedione was immediately converted under the influence of the alkaline medium into 3-(p-methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V) [3]. The latter was isolated from the reaction mixture in a yield of 45.6%, based on (III). Its semicarbazone, the same as other unsaturated semicarbazones in this series [2, 3], assumed an intense yellow color in the light, but this color vanished when the compound was dissolved in alcohol.

The catalytic hydrogenation of the ditertiary double bond in (V) was run by us using palladium catalyst and either an acid or alkaline medium. In acid medium the hydrogen absorption went rapidly and didn't slow up after 1 mole of hydrogen had been added. The absorption stopped only after 3 moles of hydrogen had been taken up, but the obtained saturated hydrogenation product did not contain the carbonyl group. In the experiment where the reduction of (V) was terminated after the absorption of 1 mole of hydrogen we obtained a difficultly separable mixture, composed of starting substance, saturated ketone and desoxy compounds. When (V) was hydrogenated in the presence of 2% potassium hydroxide the addition of hydrogen went slowly and stopped completely after the absorption of 1 mole of hydrogen. The configuration of the 3-(p-methoxyphenyl)-2-methylcyclopentanone (VI), obtained in this manner in 95.5% yield, was not established exactly by us, but if we go by the statements of Weidlich and Meyer-Delius [4] that hydrogen adds 1,4 when α,β-unsaturated ketones are hydrogenated in alkaline medium, then the methyl group and the hydrogen at C_3 should be found in the cis-position.

The subsequent conversion of (VI) to (I) was accomplished by a series of reactions, shown in sequence in the scheme given below.



The demethylation of (VI) with a mixture of HBr and CH_3COOH gave 3-(p-hydroxyphenyl)-2-methylcyclopentanone (VII) in 89.5% yield. A temporary masking of the phenolic hydroxyl, needed for the successful carrying out of the following steps, was accomplished by converting (VII) to the benzyl ether. 3-(p-Benzyloxyphenyl)-2-methylcyclopentanone (VIII) was obtained in 79% yield by heating (VII) with benzyl chloride and potash in acetophenone medium [5]. Aluminum lithium hydride was used to reduce the keto group in (VIII); the reduction was strictly stereospecific here, since only one of the two possible epimers of 3-(p-benzyloxyphenyl)-2-methylcyclopentanol (IX) with m. p. 75.5-76° was obtained in 98% yield. By analogy with the stereospecific reduction by aluminum lithium hydride of the 17-keto group in androstane derivatives [6], and judging by the fact that the tosyl ester (XIb) is stable [7], we postulate that the hydroxyl group in (VIII) is found in the cis-position to the methyl group.

In the next step we removed the benzyl radical from the benzoate of (IX), introduced earlier to temporarily protect the phenolic hydroxyl. The debenzylation was accomplished by hydrogenating (IXa) in the presence of either Pd/$BaSO_4$ or skeletal nickel catalyst in methanol. It was observed that when the catalytic debenzylation was run with palladium catalyst at elevated temperature (40-50°), as is recommended by Morris and others [8-10], the benzoate suffered partial hydrolysis with the formation of 3-(p-hydroxyphenyl)-2-methylcyclopentanol (X).

The hydrogenation of the phenolic ring in the benzoate of 3-(p-hydroxyphenyl)-2-methylcyclopentanol was run in dioxane using as catalyst 2% Pd deposited on strontium carbonate [11]. In preliminary experiments on the reduction of ethyl p-hydroxybenzoate it was established that under our conditions the ethyl ester of p-hydroxycyclohexanecarboxylic acid is formed in quantitative yield if the hydrogenation is run at a temperature of 200-220° and a pressure of 150-160 atm. These conditions also proved suitable for the exhaustive reduction of (Xa), and the 1-hexahydrobenzoate of 3-(p-hydroxycyclohexyl)-2-methylcyclopentanol (XIa) was obtained in 97% yield as a colorless liquid with b. p. 162-163° at 0.3 mm.

A new asymmetric center arises at $C^{4'}$ in the hydrogenation of (Xa), and consequently the formation of two epimeric alcohols is possible. However, our attempts to isolate them gave a negative result—the hydrogenation was strictly stereospecific here. The tosylation of (XIa) also gave but one tosylate in quantitative yield. The latter melted at 86-87° and crystallized as completely homogeneous needles.

The oxidation of (XIa) with sodium dichromate in acetic acid [12] gave 3-(4-oxocyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIIa) (an oil with b. p. 170-173° at 0.5 mm), which by saponification with alcoholic caustic was converted to 3-(4-oxocyclohexyl)-2-methylcyclopentanol (XII), also obtained as an oily liquid. Only its benzoate (XIIb) was obtained crystalline.

EXPERIMENTAL

p-Methoxyacetophenone was obtained by us without the use of inert solvents. To 342 g of anisole was added 280 g of aluminum chloride with stirring and cooling, and then 185 g of acetyl chloride was added in 2.5 hours at a temperature not exceeding +4°. The mixture was gradually warmed to 40°, stirred at this temperature for 3 hours, and then allowed to stand overnight. After decomposing the mixture with ice the excess anisole was vacuum-distilled on the water bath; the residue was distilled, collecting the fraction with b. p. 141-142° at 15 mm. We obtained 320 g of p-methoxyacetophenone (90.7%, based on acetyl chloride). M. p. 38°.

p-Methoxy-ω-bromoacetophenone (II). To a solution of 20 g of p-methoxyacetophenone in 70 ml of dry chloroform was added at room temperature and with stirring a solution of 21 g of bromine in 55 ml of chloroform. The reaction mixture was then slowly heated on the water bath. Hydrogen bromide began to evolve at 35°, and became quite violent at 40°; the color of the mixture changed from red-brown to light yellow, and the precipitate formed at first quickly disappeared. After the evolution of hydrogen bromide had ceased the mixture was allowed to cool; a precipitate of p-methoxy-ω-bromoacetophenone began to deposit at 28-30°. The reaction mass was washed with water. After drying the chloroform solution over calcium chloride the solvent was vacuum-distilled and the residue was recrystallized from methanol. We obtained 16.4 g of (II) with m. p. 70-71°. Yield 52%.

Ethyl propionylacetate (III) was obtained by the Blaise method [13, 14]; the reaction of ethylmagnesium bromide with ethyl cyanoacetate was run at a temperature not exceeding 20°.

Ethyl p-methoxyphenacylpropionylacetate (IV). To 1.8 g of sodium dust in 100 ml of ether was added with stirring in 1.5 hours a solution of 10 g of ethyl propionylacetate in 50 ml of ether and the mixture was then heated for 3 hours until all of the sodium had dissolved. The obtained sodio derivative was then treated in 40 minutes with a solution of 15.9 g of p-methoxy-ω-bromoacetophenone in 150 ml of ether. The yellow-colored reaction mixture was heated for 7 hours, and then with external cooling was treated with 40 ml of water. The ether layer was separated and after the usual treatment of the extract* we obtained 20 g of p-methoxyphenacylpropionylacetic ester (IV) as a viscous oil. It was used without further purification for the preparation of (V).

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* The "usual treatment" of extracts in an organic solvent consists in their being washed, dried, and the solvent removed by distillation.

3-(p-Methoxyphenyl)-2-methyl-2-cyclopenten-1-one (V). A mixture of 20 g of crude ethyl p-methoxyphenacylpropionylacetate and 800 ml of 2% sodium hydroxide solution was heated with stirring at 40-50° for 6 hours, at which time the ester gradually went into solution. Then the mixture was rapidly brought to the boil and boiled for 10 minutes. The oily layer that separated on cooling was extracted with ether, the ether extract was subjected to the usual treatment, and the residue (V) distilled at 142-145° at 1 mm as a colorless oil, which crystallized in the receiver. Yield 6.4 g (45.6%). M. p. 61-62° (from ethyl acetate).

Found %: C 76.97, 77.06; H 7.16, 6.81. $C_{13}H_{14}O_2$. Calculated %: C 77.2; H 6.97.

The semicarbazone with m. p. 238-239° (with decompn.) rapidly turns yellow in the light; a colorless solution is obtained when the colored compound is dissolved in alcohol.

Found %: N 16.31. $C_{14}H_{17}O_2N_3$. Calculated %: N 16.21.

3-(p-Methoxyphenyl)-2-methylcyclopentanone (VI). Ten grams of (V) was hydrogenated with 20 g of previously reduced 2% Pd/$CaCO_3$ in 300 ml of methanol, containing 0.2 g of potassium hydroxide; 1 mole of hydrogen was absorbed in 6 hours. The catalyst was filtered, the filtrate neutralized with acetic acid, the solvent distilled off, and the residue vacuum distilled. We obtained 9.55 g of highly viscous oil; b. p. 115-116° at 2 mm, n_D^{20} 1.542.

Found %: C 76.64, 76.97; H 7.94, 7.96. $C_{13}H_{16}O_2$. Calculated %: C 76.44; H 7.89.

The semicarbazone of (VI) with m. p. 217.5-218.5° does not change in the light.

Found %: C 64.39, 64.31; H 7.42, 7.21; N 16.16. $C_{14}H_{19}O_2N_3$. Calculated %: C 64.34; H 7.33; N 16.08.

3-(p-Hydroxyphenyl)-2-methylcyclopentanone (VII). A solution of 14 g of (VI) in a mixture of 280 ml of glacial acetic acid and 280 ml of hydrobromic acid (d 1.46) was refluxed in a carbon dioxide stream for 2.5 hours, after which the acetic and hydrobromic acids were removed by vacuum-distillation. The residue was dissolved in 5% sodium hydroxide solution; the obtained solution was extracted with ether and then acidified with hydrochloric acid until acid to Congo. The separated crystals were filtered and recrystallized from either ethyl acetate or 50% aqueous alcohol. We obtained 11.65 g (89.5%) of 3-(p-hydroxyphenyl)-2-methylcyclopentanone with m. p. 138-139°.

Found %: C 75.60, 75.82; H 7.47, 7.39. $C_{12}H_{14}O_2$. Calculated %: C 75.80; H 7.36.

3-(p-Benzyloxyphenyl)-2-methylcyclopentanone (VIII). A solution of 20 g of (VII) in 100 ml of acetophenone was treated at 100° with 18 g of finely divided potash and then at 140° in drops with 16.5 g of benzyl chloride. After heating at the latter temperature for 7 hours the excess benzyl chloride and the acetophenone were steam-distilled. The oily residue was rubbed with 2% potassium hydroxide solution and then recrystallized from 80% alcohol. M. p. 79-79.7°. Yield 79.4%.

Found %: C 80.92; H 7.05. $C_{19}H_{20}O_2$. Calculated %: C 81.03; H 7.19.

3-(p-Benzyloxyphenyl)-2-methylcyclopentanol (IX). To a suspension of 1.6 g of aluminum lithium hydride in 60 ml of absolute ether was added with stirring 10 g of (VIII) in 100 ml of absolute ether at such a rate that the reaction mass refluxed. The mixture was refluxed for 1 hour and then with external cooling by ice it was treated with water in drops (to decompose the excess aluminum lithium hydride) and hydrochloric acid until all of the precipitate had dissolved. The separated ether layer was subjected to the usual treatment; removal of the solvent gave 9.8 g of 3-(p-benzyloxyphenyl)-2-methylcyclopentanol with m. p. 73-74°. For analysis the substance was recrystallized from a mixture of benzene and benzine. M. p. 75.5-76°.

Found %: C 81.02, 80.89; H 8.11, 8.00. $C_{19}H_{22}O_2$. Calculated %: C 81.04; H 7.91.

3-(p-Benzloxyphenyl)-2-methylcyclopentyl benzoate (IXa) was obtained by reacting 9.5 g of (IX) with 6.5 g of benzoyl chloride in a mixture of 35 ml of dioxane and 13 ml of pyridine at room temperature. The obtained yellow oily product (12.5 g) was dissolved in 50 ml of benzene and then passed through a column containing aluminum oxide, which was then eluted with benzene. After vacuum-distillation of the solvent the residue crystallized. Recrystallized from a mixture of benzene and benzine, the substance had m. p. 70.5-71.5°.

Found %: C 81.23; H 6.74. $C_{26}H_{26}O_3$. Calculated %: C 80.9; H 6.78.

3-(p-Hydroxyphenyl)-2-methylcyclopentyl benzoate (Xa) (debenzylation). a) A solution of 3 g of (IXa) in 150 ml of methanol was hydrogenated with 3 g of 2.5% palladinized barium sulfate. When the hydrogen absorption slowed up another 2 g of catalyst was added and the hydrogenation continued until the calculated amount of hydrogen had been absorbed (6.5 hours). After removal of the catalyst and vacuum distillation (30°) of the solvent the residue (m. p. 107.5-109°) was recrystallized from a mixture of benzene and benzine. Yield 93%.

Found %: C 76.8; H 6.74. $C_{19}H_{20}O_3$. Calculated %: C 77.06; H 6.78.

The hydrogenation of (IXa) at 40° gave a mixture which after treatment with sodium bicarbonate and subsequent acidification yielded benzoic acid with m. p. 119-121° (identified by mixed melting point). In addition, recrystallization from a mixture of benzene and benzine gave two compounds with m. p. 108.8-109.5° (Xa) and with m. p. 147.3-147.7°; based on its analysis the latter is 3-(p-hydroxyphenyl)-2-methylcyclopentanol (X).

Found %: C 75.26, 74.83; H 8.04, 8.25. $C_{12}H_{16}O_2$. Calculated %: C 74.96; H 8.39.

b) To a suspension of 1 g of skeletal nickel catalyst in 40 ml of methanol, previously saturated with hydrogen, was added a solution of 0.5 g of (IXa) in 30 ml of methanol, and the whole hydrogenated at atmospheric pressure. The amount of hydrogen absorbed in 25 minutes was 35 ml (compared to theoretical 32 ml). We obtained 0.38 g of (Xa) with m. p. 107-108°.

3-(p-Hydroxycyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIa). Into a stainless steel autoclave fitted with stirrer was placed 10 g of benzoate (Xa), 5 g of 2% Pd/$SrCO_3$ catalyst and 300 g of peroxide-free dioxane. After removal of air the autoclave was filled with hydrogen to a pressure of 110-120 atm, then gradually heated to 200-220° and kept at this temperature for 2 hours. Here the pressure in the autoclave rose to 150-160 atm, while the residual pressure in the autoclave after its cooling was 90 atm. After distilling off the solvent the obtained residue (viscous colorless oil) was vacuum-distilled; b. p. 162-163° at 0.3 mm. Yield 9.7 g.

Found %: C 73.9, 74.08; H 10.55, 10.39. $C_{19}H_{32}O_3$. Calculated %: C 74.04; H 10.31.

(XIb) Tosylate, m. p. 86-87°.

Found %: C 67.46; H 8.35; S 6.99. $C_{26}H_{38}O_5S$. Calculated %: C 67.49; H 8.28; S 6.93.

3-(4-Oxocyclohexyl)-2-methylcyclopentyl hexahydrobenzoate (XIIa). A solution of 2 g of (XIa) in 20 ml of glacial acetic acid (stable to CrO_3) was treated with a solution of 0.7 g of sodium dichromate in 7 ml of acetic acid; the temperature was kept at 20°. The mixture was stirred for another hour and then allowed to stand for 12 hours. The reaction mass was diluted with 100 ml of water and the acetic acid and part of the water were vacuum-distilled. The residue was diluted with water and then extracted with ether. After the usual treatment of the ether extract the residue was vacuum-distilled. We obtained 1.85 g (92.5%) of a noncrystallizing oil with b. p. 170-173° at 0.4 mm.

Found %: C 74.30; H 9.81. $C_{19}H_{30}O_3$. Calculated %: C 74.07; H 9.81.

(XIIa) Semicarbazone, m. p. 167-168°.

Found %: C 66.10; H 9.23; N 11.65. $C_{20}H_{33}O_3N_3$. Calculated %: C 66.08; H 9.15; N 11.56.

3-(4-Oxocyclohexyl)-2-methylcyclopentanol (XII) was obtained by saponifying its hexahydrobenzoate with methanolic potassium hydroxide with heating for 2.5 hours. The methanol was then vacuum-distilled, and the residue was diluted with water and extracted with ether. After the usual treatment we obtained 3.65 g of yellowish oily substance. To purify the substance its chloroform solution was passed through a column containing aluminum oxide, from which (XII) was eluted using 500 ml of chloroform. Removal of the chloroform by distillation (at the end in vacuo) left a colorless oil.

Found %: C 73.34, 73.50; H 10.31, 10.57. $C_{12}H_{20}O_2$. Calculated %: C 73.43; H 10.22.

3-(4-Oxocyclohexyl)-2-methylcyclopentyl benzoate (XIIb). A solution of 2.85 g of (XII) in 15 ml of pyridine was treated at 20° with 2.4 g of benzoyl chloride. The next day the reaction mass was poured into water, acidified with hydrochloric acid until acid to Congo, and stirred for 2 hours. The obtained precipitate was filtered, washed with water, then with sodium bicarbonate solution, again with water, dried in a vacuum-desiccator, rubbed with a small amount of hexane to remove oily impurities, and finally recrystallized from 70% ethanol. We obtained 3.66 g (84%) of the benzoate with m. p. 76-76.5°.

Found %: C 76.20; H 8.07. $C_{19}H_{24}O_3$. Calculated %: C 75.96; H 8.07.

The semicarbazone of the benzoate has m. p. 163-164° (with decompn.; from alcohol).

SUMMARY

Starting with p-methoxyacetophenone and ethyl propionylacetate we synthesized 3-(4-oxocyclohexyl)-2-methylcyclopentanol.

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Received November 1, 1956

ANALOGS OF STEROID HORMONES

II. SYNTHESIS OF 6-(2-METHYL-3-HYDROXYPENTYL)-$\Delta^{1(9)}$-OCTALONE

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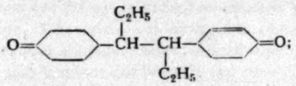
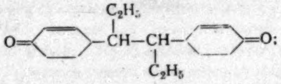
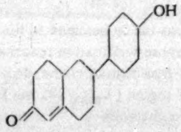
Extensive investigations made in the field of analogs of follicular hormones have revealed that there exists a large number of compounds, lacking the steroid structure, but possessing all of the physiological properties of the natural hormones. Many of these so-called "synthetic estrogens" have a physiological activity that equals or even exceeds the activity of the natural hormones; some of them, as for example diethylstilbestrol, have found wide application in clinical practice.

In contrast to this, studies devoted to a search for analogs of other steroid hormones have not received sufficient development. For example, until now, only several nonsteroid compounds have been described which have proved capable of showing to variable degree the physiological reactions characteristic for the male sex hormone. Included among them are 3-(oxocyclohexyl)-4-(oxocyclohexenyl)hexane, 3,4-di-(4-oxocyclohexenyl)-hexane [1], 6-(4'-hydroxycyclohexyl)-$\Delta^{1(9)}$-2-octalone [2, 3], and some compounds analogous to the latter.



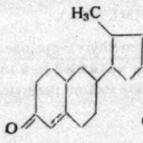




These examples indicate that the androgenic activity is apparently not strictly specific, and that it is linked only with the androstane and perhydrochrysene (the so-called D-homosteroids) structures.

In order to make further systematic searches for analogs of the steroid hormones it is necessary to have additional information on the relationship between physiological properties and structure, and in particular to know to what extent changes in the skeleton of steroid hormones are permissible.

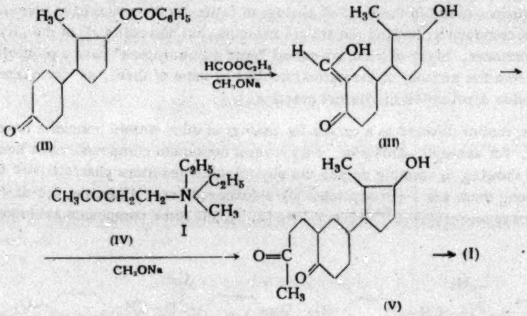
In connection with this we made a study of the synthesis of 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I). It is possible to regard this compound as being an analog of the androgenic hormones, lacking the ring C and the angular methyl group at C_{10}.



(I)

Based on the examples of 19-nortestosterone [4], 19-norprogesterone [5] and 19-nordesoxyticosterone [6], it is known that an angular methyl group between rings A and B is not essential for the appearance of the corresponding hormonal activity.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I) was obtained from the earlier synthesized [7] benzoate of 3-(4-oxocyclohexyl)-2-methylpentanol (II). To convert (II) to the octalone derivative we used the method of Robinson and co-workers [8], widely used in recent years for introducing into cyclic ketones a new cycle, containing a keto group with a conjugated double bond. The method consists of the condensation of the starting ketone with methyl vinyl ketone in the presence of a base, followed by closure of the formed diketone into a new cycle on the type of a crotonic condensation. Instead of the unstable and easily polymerized methyl vinyl ketone it is also possible to use diethylamino-2-butanone methiodide (IV) in this reaction, which under the conditions of the condensation reaction is converted into methyl vinyl ketone. Since it is known [8] that the introduction of a formyl radical in the α-position to the keto group facilitates the addition of methyl vinyl ketone, we first converted (II) to its formyl derivative (III), which was then condensed with (IV).



The reaction of (II) with ethyl formate was run in benzene in the presence of sodium methylate. The formation of (III) was accompanied by a side transesterification reaction, since ethyl benzoate was isolated from the reaction mixture. The obtained 3-(3-hydroxymethylene-4-oxocyclohexyl)-2-methyl-1-cyclopentanol (III) showed an absorption maximum in the UV region (λ_{max} 281 mμ) characteristic for the formyl grouping [9], and gave an intense violet color with ferric chloride.

The reaction of (III) with (IV) in the presence of sodium methylate gave 3-[3-(γ-oxobutyl)-4-oxocyclohexyl]-2-methylcyclopentanol (V). To cyclize (V) we used potassium hydroxide in methanol solution at room temperature. The oily substance isolated from the reaction mixture was purified by chromatographing on aluminum oxide, followed by recrystallization from ether. 6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone (I) crystallized as slender needles with m. p. 107.5-109.5°. It shows an absorption maximum at 238 mμ. Its p-nitrobenzoate has m. p. 106-108°.

The biological testing of 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone, done by I. N. Lektorskii (Pharmacology Section of the All-Union Chemical Pharmaceutical Research Institute), revealed that it is inactive in dosage up to 7 mg when tested for comb-growth on roosters.

EXPERIMENTAL

3-(3-Hydroxymethylene-4-oxocyclohexyl)-2-methyl-1-cyclopentanol (III). To a suspension of sodium methylate (from 0.3 g of sodium) in 7 ml of benzene was added in a stream of nitrogen at room temperature with stirring 7.5 g of ethyl formate in drops. After the sodium methylate had dissolved, to the yellow reaction mass with ice-cooling was added a solution of 1 g of 3-(4-oxocyclohexyl)-2-methyl-1-cyclopentanol benzoate in 6 ml of benzene, and the mixture was stirred for 20 hours. The resulting formyl compound was repeatedly extracted with 2% sodium hydroxide solution. The alkaline extracts were treated with ether and then acidified with hydrochloric acid until acid to Congo. The obtained oily substance was extracted with chloroform. After treating the chloroform extract in the usual manner the solvent was vacuum-distilled in a nitrogen stream at a bath temperature not exceeding 30°. We obtained 0.75 g of residue as a yellow oil. The oil gives an intense violet color with ferric chloride and has λ_{max} 281 mμ in the ultraviolet region. This substance was used without further purification in the next step.

The oily residue, obtained in an amount of 0.35 g after distilling off the solvents from the combined benzene solution and ether extract, distilled at 222°. Its saponification with methanolic potassium hydroxide solution gave benzoic acid (m. p. 119-120°).

3-[3-(γ-Oxobutyl)-4-oxocyclohexyl]-2-methyl-1-cyclopentanol (V). To a solution of sodium methylate (from 0.2 g of sodium and 7.5 ml of methanol) in a stream of nitrogen was added a solution of 0.75 g of (III) in 7 ml of methanol, and the mixture stirred for 30 minutes at room temperature. Then the mixture was cooled in an ice-salt mixture and treated in drops with a solution of diethylamino-2-butanone methiodide (from 1.3 g of diethylamino-2-butanone and 2 g of methyl iodide) in 5 ml of methanol. After stirring for 15 minutes the cooling bath was removed and the reaction mass was allowed to stand at room temperature for 18 hours. Then with cooling it was acidified with 10% hydrochloric acid, diluted with water, and extracted with chloroform. After the usual treatment of the chloroform extract and removal of the solvent by distillation we obtained 0.85 g of an oily residue, containing 3-[3-(γ-oxobutyl)-4-oxocyclohexyl]-2-methylcyclopentanol (does not react to color test with ferric chloride). It was used without purification in the subsequent reactions.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone. A mixture of 0.5 g of (V), 2 g of potassium hydroxide and 50 ml of methanol was stirred for 2.5 hours at room temperature. Then the reaction mass was cooled, carefully neutralized with dilute hydrochloric acid, and the mixture extracted with chloroform. The chloroform extract was washed with water, and then dried over anhydrous sodium sulfate. After distilling off the chloroform (at the end in vacuo) we obtained 0.45 g of a yellow oily residue, having λ_{max} 238 mμ in the UV region. This residue was dissolved in 10 ml of dry benzene and the solution passed through a column containing neutral aluminum oxide, diluted with ethyl acetate. The crystalline fractions, obtained on washing the column with a mixture of benzene and ether (1 : 1), were combined and purified by recrystallization from ether. The 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone was obtained as needles with m. p. 107.5-109°; λ_{max} 238 mμ log E 4.20.

Found %: C 77.23; H 9.71. $C_{16}H_{24}O_2$. Calculated %: C 77.37; H 9.72.

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone p-nitrobenzoate. To a solution of 0.2 g of the oily substance, obtained after cyclization, in 3 ml of dry pyridine was added with ice-water cooling 0.19 g of p-nitrobenzoyl chloride. The next day the reaction mixture was poured into water and stirred for 1.5 hours. The obtained oily substance was extracted with ether. The ether extract was washed with water, dilute hydrochloric acid, soda solution, again with water, and then dried over sodium sulfate. Removal of the ether by distillation left 0.27 g of oily substance, which crystallized on standing. Two recrystallizations from ether gave 6-(2-methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone p-nitrobenzoate with m. p. 106-108°.

Found %: C 69.62; H 6.79. $C_{23}H_{27}O_5N$. Calculated %: C 69.5; H 6.85.

SUMMARY

6-(2-Methyl-3-hydroxycyclopentyl)-$\Delta^{1(9)}$-2-octalone was synthesized from 3-(4-oxocyclohexyl)-2-methylpentanol.

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S. Ordzhonikidze All-Union Chemical
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Received November 1, 1956

•Original Russian pagination. See C. B. Translation.

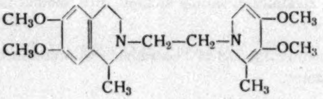
ALKALOIDS OF SALSOLA RICHTERI

VI. STRUCTURE OF SALSAMINE

N. F. Proskurnina

In an earlier paper we had described the isolation of the alkaloid salsamine from the above-ground portions of the Central Asiatic plant Salsola Richteri, the analysis of which gave values lying between those calculated for the formulas $C_{12}H_{17}O_2N$ and $C_{13}H_{19}O_2N$ [1]. In this paper we give the results of a more detailed study of salsamine. It was established that this base when purified more carefully is optically inactive and had m. p. 165-167°. Based on its analysis and determination of the molecular weight (428) this substance should be assigned the formula $C_{26}H_{36}O_4N_2$. All four oxygen atoms in salsamine are found present as methoxy groups. In addition to salsamine, we also isolated optically active base, isomeric with salsamine, from the mother liquors.

The oxidation of salsamine and of its optically active isomer with permanganate gave the same optically inactive oxidation product having a neutral character ($C_{24}H_{28}O_6N_2$). The composition and properties of this latter substance show that the oxidation of salsamine proceeds with the cleavage of two carbon atoms and the formation of lactam groups similar to what occurs in the oxidation of salsolidine under the same conditions [2]. On this basis it can be postulated that salsamine and its isomer are the respective condensation products of dl-salsolidine and l-salsolidine with dichloroethane, which was confirmed experimentally. The condensation of dl-salsolidine with dichloroethane gave a base identical with salsamine, while the condensation of l-salsolidine with dichloroethane gave the dextrorotatory base isomeric with salsamine. Both bases can be depicted by the formula given below.



Consequently, both salsamine and its optically active isomer are apparently not found as such in the plant, but are formed in the process of extracting the alkaloids from the plant with dichloroethane.

EXPERIMENTAL

The earlier described procedure [1] was used to isolate salsamine from the mother liquors of the total alkaloids found in Salsola Richteri. The separation of salsamine and its optically active isomer was effected on the basis of the different solubility of their hydrochlorides. When a mixture of the hydrochlorides is recrystallized from alcohol the first to crystallize is the more difficultly soluble salsamine hydrochloride, which after purification has m. p. 242-247°. Evaporation of the mother liquors to small volume gave an amorphous hydrochloride, which after boiling with acetone was dissolved in alcohol. Dilution of the alcohol solution with 10 volumes of acetone, followed by standing, gave a powder-like crystalline precipitate. After the hydrochloride was purified by recrystallization from alcohol it had m. p. 196-198°. The free base isolated from the hydrochloride, after recrystallization from acetone, had m. p. 96-98° and $[\alpha]_D$ +37.5° (c 2.0, in alcohol).

Found %: C 71.03; H 8.19; N 6.43; CH_3O 27.4. $C_{26}H_{36}O_4N_2$. Calculated %: C 70.90; H 8.18; N 6.36; $4CH_3O$ 28.1.

Oxidation of salsamine with permanganate in acetone solution. To a solution of 0.5 g of salsamine with m. p. 165-167° in 50 ml of acetone was added in drops an acetone solution of $KMnO_4$ (0.92 g in 100 ml). The MnO_2 precipitate was filtered and washed with acetone. The acetone solution was reduced to a small volume. The obtained precipitate of oxidation product was recrystallized from alcohol (m. p. 212-214°).

Found %: C 65.21; H 6.29; N 6.47. $C_{24}H_{28}O_5N_2$. Calculated %: C 65.45; H 6.36; N 6.36.

Oxidation of isomer of salsamine with permanganate in acetone solution. The base (0.5 g) with m. p. 96-98° and $[\alpha]_D$ +37.5° was oxidized with permanganate under the conditions of the preceding experiment. A mixture of the isolated oxidation product (m. p. 212-214°) with the oxidation product of salsamine did not depress the melting point.

Condensation of dl-salsolidine with dichloroethane. A solution of 2 g of dl-salsolidine with m. p. 52-53° in 50 ml of dichloroethane was refluxed in the presence of 2 g of $NaHCO_3$ for 8 hours. The filtered solution was vacuum-distilled to dryness, the residue dissolved in 5% hydrochloric acid, the solution filtered, and the free base isolated by the addition of $NaHCO_3$ and subsequent extraction with ether. After we distilled off the ether the crystalline residue was boiled with acetone, and then recrystallized several times from alcohol (m. p. 165-167°). Its mixture with salsamine did not depress the melting point.

Found %: C 70.75; H 8.20; N 6.52. $C_{26}H_{36}O_4N_2$. Calculated %: C 70.90; H 8.18; N 6.36.

The hydrochloride of the condensation product obtained from dl-salsolidine had m. p. 242-247°.

Condensation of l-salsolidine with dichloroethane. Two grams of l-salsolidine with m. p. 57-60° and $[\alpha]_D$ −59.7° was condensed with dichloroethane under the conditions of the preceding experiment. After the base was purified by recrystallization from alcohol it had m. p. 96-98° and $[\alpha]_D$ +37.5° (*c* 2.0, in alcohol).

The hydrochloride of the condensation product of l-salsolidine with dichloroethane was obtained as an amorphous mass by treating the free base with alcoholic hydrochloric acid. Dissolving the amorphous hydrochloride in a small amount of alcohol, followed by dilution with acetone, gave the crystalline hydrochloride (m. p. 196-198°).

SUMMARY

1. After isolating the main alkaloids of Salsola Richteri, still another new base, isomeric with salsamine, was isolated from the mother liquors.

2. The condensation of dl-salsolidine and of l-salsolidine with dichloroethane gave respectively salsamine and its optically active isomer.

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Received January 7, 1957

ACONITE ALKALOIDS

IX. ALKALOIDS OF ACONITUM EXCELSUM

T. F. Platonova, A. D. Kuzovkov and P. S. Massagetov

The alkaloids of the tall aconite (Aconitum excelsum Rehb.) were studied by S. Iu. Iunosov, who briefly mentioned in his paper [1] the isolation of mesaconitine and two bases, characterized only by their melting points (265-267°, and about 100°).

We investigated the roots of the tall aconite. The material was collected in T'ien-Shang in the fall after the above-ground portion of the plant had withered. The investigated sample contained 3% of mixed alkaloids, the paper-chromatographing of which showed the presence of only three substances (R_f 0.66, 0.49 and 0.38). Separation of the mixture permitted isolating lappaconitine (R_f 0.66) and two new alkaloids (R_f 0.74 and 0.76), which were not found when the total alkaloids were chromatographed on paper and for which we propose the name of acsine and acsinatine. The dry roots were shown to contain 1.6% lappaconitine, 0.016% acsine and 0.002% acsinatine. Consequently, the investigated material contained at least five bases. The substances, having R_f 0.49 and 0.38, could not be isolated in the pure state.

Acsine, $C_{21}H_{29}O_5N$, contains two alcoholic OH groups, one acetoxy group, and apparently an ether linkage. Acsinatine, $C_{21}H_{27}O_4N$, contains one alcoholic OH group, one keto group, and the same as acsine, one acetoxy group. Saponification of the acetoxy groups from acsine and acsinatine gave amino alcohols, respectively acsinidine, $C_{19}H_{27}O_4N$, and acsinatidine, $C_{19}H_{25}O_3N$.

The above-ground portions of the tall aconite, collected in T'ien-Shang in the preflowering stage, contained 0.5% of noncrystalline total alkaloids; the chromatographing of the total alkaloids on paper revealed the presence of three substances (R_f 0.64, 0.49 and 0.38). We were able to isolate only lappaconitine (0.06%) from this mixture of substances.

EXPERIMENTAL

Isolation of Alkaloids

Forty-five kilograms of dried and ground roots of Aconitum excelsum was moistened with 5% soda solution and then exhaustively extracted with dichloroethane. The alkaloids were extracted from the dichloroethane solution with 5% H_2SO_4. The sulfuric acid extract was treated with a small amount of ether; then the mixture with vigorous shaking was made alkaline with 5% soda solution. The crystalline precipitate (1025 g, portion A) was filtered; extraction of the filtrate with ether yielded 357 g of an oily mixture of bases (portion B). When chromatographed on Leningrad Factory No. 2 paper (solvent—butanol, saturated 5% CH_3COOH, temperature around 20°, developer-Dragendorff's reagent) portion A was shown to contain one substance (R_f 0.66) while portion B was found to contain three substances (R_f 0.66, 0.49 and 0.38).

The mixture of crystalline bases (portion A) (1025 g) was dissolved in 6 liters of 5% hydrochloric acid and the solution treated with an excess of saturated $NaClO_4$ solution. The perchlorate precipitate, obtained as an oil, was separated from the aqueous solution, washed with a small amount of water, and then dissolved with heating in 2 liters of CH_3OH. The crystalline precipitate of lappaconitine perchlorate obtained on cooling was purified by refluxing with 1 liter of CH_3OH; yield 800 g, m. p. 250°. The lappaconitine was identified by its direct comparison with the lappaconitine obtained from Aconitum oriental [2]. After removal and purification of the lappaconitine perchlorate, the aqueous and methanolic solutions were worked up to yield 315 g of an oily mixture of bases, which were separated by their basicity into 18 fractions. When chromatographed on paper, all of the fractions were found to contain only lappaconitine (R_f 0.66), and here 80 g of it was isolated.

The tarry mixture of alkaloids (portion B) (357 g) was dissolved in 400 ml of 5% H_2SO_4; fractional alkalization with 19 equal portions of caustic and extraction with ether gave 19 fractions. After rubbing these with ether we were able to isolate 5.5 g of lappaconitine from fractions 9-14, and 6.5 g of acsine from fractions 15-18. From the ether mother liquors after removal of the acsine a second division of the alkaloids by basicity into 10 fractions yielded 0.5 g of acsine and 1.2 g of acsinatine. From the 19th fraction after a second division of the alkaloids by basicity we isolated 1.9 g of the difficultly water-soluble acsine sulfate and 0.3 g of acsinatine.

When heated slowly acsine melts at 182-185°, and when heated rapidly it melts at 192-195°; it is difficultly soluble in ether, acetone and alcohol, and somewhat more soluble in chloroform; R_f 0.74 $[\alpha]_D^{20}$ +4.2° (c 10.0, CH_3OH). Its infrared spectrum shows bands at 3704 cm^{-1} and 3333 cm^{-1} (OH groups), while in the 1650-1750 region only one band is found at 1737 cm^{-1} (ester carbonyl).

Found %: C 66.90, 66.50; H 8.14, 7.90; N 3.70, 3.58; OH 8.66. $C_{21}H_{29}O_5N$. Calculated %: C 67.18; H 7.78; N 3.73; OH 9.05.

Acsine sulfate was obtained by treating the free base with 5% H_2SO_4, m. p. 220° (decompn.).

Found %: C 59.76, 59.31; H 7.00, 6.99; N 3.38; S 3.73. $C_{21}H_{29}O_5N \cdot H_2SO_4$. Calculated %: C 59.41; H 7.12; N 3.30; S 3.77.

Acsinatine melts at 246-247°, R_f 0.76, is difficultly soluble in ether, alcohol and acetone, and readily soluble in chloroform; it fails to give crystalline salts with the common organic and inorganic acids. Its infrared spectrum shows bands at 3704 cm^{-1} (OH), 1737 cm^{-1} (ester carbonyl) and 1724 cm^{-1} (keto group).

Found %: C 70.99, 70.90; H 7.59, 7.65; N 4.06, 4.29; OH 5.04. $C_{21}H_{27}O_4N$. Calculated %: C 70.57; H 7.61; N 3.91; OH 4.74.

Saponification of Acsine and Acsinatine

A solution of 0.5 g of acsine and 0.4 g of NaOH in 20 ml of CH_3OH was refluxed for 1 hour. The residue after removal of the alcohol was dissolved in 5 ml of water. Extraction with chloroform gave 0.3 g of oily substance, which crystallized when rubbed with acetone. We obtained 0.1 g of acsinidine, m. p. 248-249.5° (from aqueous acetone).

Found %: C 68.60, 68.03; H 8.13, 7.84; N 4.07, 3.76. $C_{19}H_{27}O_4N$. Calculated %: C 67.44; H 8.16; N 4.29.

From 0.5 g of acsinatine, after saponification and treatment in the same manner as described above, we obtained 0.15 g of acsinatidine, m. p. 225-227° (from aqueous acetone).

Found %: C 72.24, 71.79; H 8.31, 8.31; N 3.92, 3.82. $C_{19}H_{25}O_3N$. Calculated %: C 72.35; H 7.98; N 4.44.

Acsinatidine hydrochloride was obtained by mixing alcohol solutions of the free base and hydrogen chloride. The addition of ether gave a crystalline precipitate, m. p. 284-285°.

SUMMARY

From the tall aconite (Aconitum excelsum Rehb.) we isolated lappaconitine and two new alkaloids—acsine, $C_{21}H_{29}O_5N$, and acsinatine, $C_{21}H_{27}O_4N$.

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Received January 8, 1957

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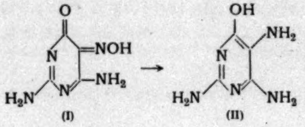
*Original Russian pagination. See C. B. Translation.

ELECTROLYTIC REDUCTION OF 2,4-DIAMINO-5-ISONITROSO-6-HYDROXYPYRIMIDINE

V. M. Berezovskii and Iu. P. Sobolev

The chemical and catalytic reduction of nitroso groups in pyridine compounds has been discussed in considerable detail in the literature, in particular for 2,4-diamino-5-isonitroso-6-hydroxypyrimidine [1, 2], which has importance in the synthesis of folic acid. However the method of electrolytic reduction of nitrosopyrimidines has been studied but slightly. Among the few studies in this field, mention should be made of the electroreduction of 3-methyl-4-amino-5-isonitroso-2,6-dihydroxypyrimidine at a lead cathode in 60% sulfuric acid [3].

In this paper we studied the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine (I) in both acid and alkaline media; the yield of 2,4,5-triamino-6-hydroxypyrimidine (II) was 77-80%.



The reduction of aromatic nitroso compounds usually proceeds in higher yield (93-97%) [4-6].

EXPERIMENTAL

The apparatus used for the reduction was a diaphragmed porcelain beaker, containing the cathode as a perforated metal cylinder or spiral tube, a coil for cooling, and a stirrer. In the anodic section was placed either a lead or a nickel anode (the first for acid, and the second for alkaline reduction), and it was filled with either 10% sulfuric acid or 10% sodium hydroxide solution.

In acid medium the electroreduction of 10 g of a suspension of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine was run with stirring in a 250 ml diaphragmed beaker containing 150 ml of hydrochloric acid solution (of variable concentration). On conclusion of reduction the solution was filtered, evaporated in vacuo to a volume of 80 ml, diluted with water to 250 ml, and poured into 30 ml of 50% sulfuric acid; here the sulfate of 2,4,5-triamino-6-hydroxypyrimidine with one mole of crystallization water crystallized rapidly. In this way over 95% of the 2,4,5-triamino-6-hydroxypyrimidine present in the reaction solution was isolated; the substance remaining in solution was not included in calculating the yields.

In alkaline medium the electroreduction of 5 g of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine dissolved in 60 ml of 1% sodium hydroxide solution was run with stirring in a 110 ml diaphragmed beaker. On conclusion of reduction the solution was filtered into 30 ml of 50% sulfuric acid, and the 2,4,5-triamino-6-hydroxypyrimidine was isolated as the sulfate.

In different experiments we studied the influence of the current density, the temperature and the cathode material, and in hydrochloric acid also the concentration of the acid, on the reaction for the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine.

Since the reduction in acid medium took place in a heterogeneous medium, then, as a rule, the experiments were run with a 100% excess of current, while in homogeneous alkaline solution it proved sufficient to use a 20% excess of the current when compared to the theoretical.

Effect of current density on yield of 2,4,5-triamino-6-hydroxypyrimidine. Varying the current density in a wide range (from 3 to 17 amp/sq dm) exerts very little effect on the yield when the reduction is run in acid medium (Table 1); reduction at 25 amp/sq dm proceeds slowly and in poor yield, which is apparently associated with a strong polarization of the cathode. In alkaline medium a change in the current density from 1 to 25 amp/sq dm is practically without effect on the yield of amino compound.

TABLE 1

Influence of Current Density on Yield of 2,4,5-Triamino-6-Hydroxypyrimidine

a) Experiments in acid medium using Pb cathode in 10% hydrochloric acid at 40°

Current density (amp/sq dm)	2	3	5	7	9	11*	17*	25*
Yield of substance (%)	65.0 (150% current)	74.0	75.1	77.5	77.4	76.5	79.2	56.6 (1000% current)

b) Experiments in alkaline medium using a Pb cathode at 30°

Current density (amp/sq dm)	1	2	4	6	8	10	15	20	25
Yield of substance (%)	72.0	69.5	72.0	74.4	75.3	72.0	74.0	73.3	74.7

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* At a current density of 11 amp/sq dm and higher the area of the cathode used was reduced in half in order to have sufficient time to dissolve the starting product.

Influence of cathode material. The yield of 2,4,5-triamino-6-hydroxypyrimidine depends on the hydrogen overvoltage at the different metal cathodes (Pb and Zn > Cu > Fe); the low yield using a mercury cathode can be explained by its specific state. The yield of substance in alkaline medium depends but slightly on the cathode material. Using a zinc or mercury cathode the yield of substance is found to depend directly on the amount of electricity passed through.

Electroreduction with the addition of either tin or zinc salts, used as promoters, led to a slight (3-4%) increase in the yield of substance when a lead cathode was used.

TABLE 2

Influence of Cathode Material on Yield of 2,4,5-Triamino-6-Hydroxypyrimidine (at 40° and a Current Density of 7-8 amp/sq dm)

Cathode material	Hg	Zn	Sn	Pb	Cu	Ni	Fe
Yield of substance in 10% hydrochloric acid (in %)	47.1	80.0, 81.6, 75.1	79.5	78.0, 78.2, 77.5	70.2	69.0	65.8
Yield of substance in alkaline medium (%)	42.9 (75.5 with 200% current)	31.8 (66.8 with 200% current)	59.3	77.2	77.3	71.4	—

The experiments on the reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine in hydrochloric acid of variable concentration are given in Table 3.

TABLE 3

Influence of Hydrochloric Acid Concentration on Yield of 2,4,5-Triamono-6-Hydroxypyrimidine (with a Current Density of 7 amp/sq dm at a Pb Cathode)

Hydrochloric acid concentration (%)	Yield of substance (%)		
	40°	60°	80°
5	57.4	74.0	
10	78.2, 77.5	69.5, 66.8	35.8
17	66.0		
36	21.1		

The influence of temperature was studied in the experiments using a lead cathode: in 10% hydrochloric acid at a current density of 7 amp/sq dm, and in alkaline solution at a current density of 8 amp/sq dm. The results of the experiments are shown in Fig. 1.

Yield based on the current. When the reduction was run in 10% hydrochloric acid at 40° the yield based on the current was 95% (when 70% of the theoretically required amount of electricity was passed through). When the reduction was run in 5 and 10% hydrochloric acid at 60° the yield based on the current decreased to 83.5%.

The relationship between the yield based on the current and the amount of electricity passed through when the reduction is carried out in an alkaline medium is shown in Fig. 2.

As had been shown by us, because of the tendency for hydrolysis of the amino group the yield of the pyrimidine amino compound (II) is greatly reduced with increase in both acid concentration and in temperature (Fig. 1) when 2-4-diamino-5-isonitroso-6-hydroxypyrimidine (I) is subjected to electrolytic reduction in an acid medium. The optimum temperature is about 40° or slightly higher. It should be mentioned that the formed 2,4,5-triamino-6-hydroxypyrimidine is stable under the reduction conditions, and its yield remains practically constant with increase in both the current density and the amount of electricity passed through.

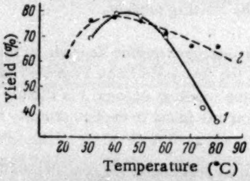

Fig. 1. Relationship between the yield of 2,4,5-triamino-6-hydroxypyrimidine and the temperature. 1) In acid medium, 2) in alkaline medium.

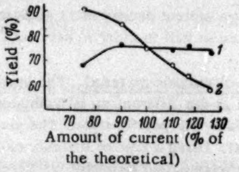

Fig. 2. Relationship between the yield of 2,4,5-triamino-6-hydroxypyrimidine and the amount of electricity (in alkaline medium, current density 6 amp/sq dm, temperature 30°). 1) yield of substance, 2) yield based on the current.

The electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine (I) in alkaline medium to 2,4,5-triamino-6-hydroxypyrimidine (II) proceeds without the formation of the by-products characteristic for the reduction of nitro compounds in alkaline medium. This is due to the fact that when the electroreduction is run in alkaline medium the o-nitrosohydroxydiaminopyrimidine (I) reacts in the form of the quinone hydroxyimine, as had been shown for the catalytic reduction of this compound [2] and as is characteristic for o- and p-isonitrosophenols. The influence of the temperature factor in alkaline medium is expressed to a much lesser degree than in acid medium (Fig. 1).

A low yield of 2,4,5-triamino-6-hydroxypyrimidine in hydrochloric acid medium can be explained by the hydrolytic cleavage of the amino group from 2,4-diamino-5-isonitroso-6-hydroxypyrimidine with the formation of 2-amino-4,6-dihydroxy-5-nitrosopyrimidine [7].

SUMMARY

The electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine in either acid or alkaline medium proceeds with the formation of 2,4,5-triamino-6-hydroxypyrimidine. It was shown that the material of the cathode exerts an influence on the yield based on the current when the electrolytic reduction of 2,4-diamino-5-isonitroso-6-hydroxypyrimidine is run in acid medium.

This is not observed when the electroreduction is run in alkaline medium.

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Received January 10, 1957

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DETERMINATION OF THE NUMBER OF ELECTRONS PARTICIPATING IN THE PROCESS FOR THE REDUCTION OF STYPTICINE AT A DROPPING MERCURY ELECTRODE. II

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The basic equations of polarography can be used for the determination of the number of electrons participating in a reaction at the dropping-mercury electrode. However this method is not applicable if the studied process is irreversible. A number of papers have been published in recent years on determining the number of electrons participating in an electrode reaction with the aid of coulometric methods [1-6]. A method that is extremely convenient and simple in this respect is that of polarographic coulometry, the essence of which is that the amount of reduced substance is divided by the amount of electricity. The number of moles of reduced substance is determined by the decrease in the limiting current with time. Several methods can be used to calculate the number of electrons participating in the process. Because of the simplicity of the calculations, the logarithmic [5] and arithmetical mean [6] methods possess the greatest interest.

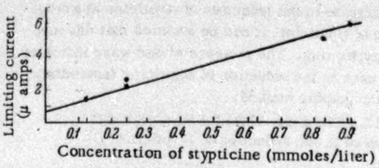
To calculate the number of electrons n by the logarithmic method it is convenient to use the formula

$$n = \frac{I_0}{c_0} \cdot \frac{K}{222 \cdot 10^3 \cdot v}\,. \tag{1}$$

where: I_0 is the limiting current (in μ amp), c is the initial concentration of the substance (in mmole/liter), v is the electrolyte volume (in ml), and $K = \frac{t}{\log \frac{h_0}{h_t}}$. The value K is obtained by the following transformations. Taking into consideration that $\log \frac{I_0}{I_t} = \frac{1}{K} \cdot t$ [5], we find that $K = \frac{t}{\log \frac{I_0}{I_t}}$, while on the basis of the equality of the ratios $\frac{I_0}{I_t} = \frac{h_0}{h_t}$, where: h is the height of the polarographic wave (in mm), and t is the time (in sec), we find that $K = \frac{t}{\log \frac{h_0}{h_t}}$. The formula used for calculation by the arithmetical mean method can be depicted in the following form

$$n = \frac{M}{F} \cdot t \cdot \frac{h_0 + h_t}{h_0 - h_t} \cdot \frac{I_0}{2vc}\,, \tag{2}$$

where: M is the molecular weight of the reacting substance, F is 96,500 coulombs, t is the time (in sec), h_0 and h_t are the heights of the polarographic wave (in mm), I_0 is the limiting current (in μ amp), v is the volume (in ml), and c is the concentration (in μg/ml).



Linear relationship existing between the value of the limiting current and the concentration of stypticine in solution at pH 8.02 and 2.61.

The arithmetical mean method of calculation makes it possible to check in a simple manner the calibration of the mirror galvanometer — a necessary value for obtaining a true diffusion current in μ amps.

The method of polarographic coulometry was checked by us on the examples of determining the number of electrons participating in the process for the reduction of p-nitroaniline, cadmium nitrate, cobalt nitrate and the alkaloid stypticine at a dropping-mercury electrode, in which connection the data obtained by us for p-nitroaniline, cadmium nitrate and cobalt nitrate agree with the results of [6].

The linear relationship existing between the values of the diffusion currents and the corresponding concentration of stypticine at pH 8.02 and 2.61 is shown in the Figure.

Taking into consideration the fact that the values of the limiting currents at various pH show very little fluctuation, it is possible to calculate their mean values for each concentration and to plot them on the graph. In this case also it is possible for us to establish that a linear relationship exists between the values of the limiting currents and the concentrations of stypticine in solution, which is expressed by the equation of a straight line. It should be mentioned that Kirkpatrick [7] also established that a linear relationship exists between the value of the diffusion current and the concentration of stypticine in solution.

EXPERIMENTAL

For running the polarographic coulometry experiments we used the vessel proposed by Stromberg and Markacheva [5] and modified somewhat by us. The vessel is a glass tube with a diameter of 5-6 mm and a length of 8 cm; in its lower part the electrolyzer is connected to a small vessel, having a hollow tap for draining off the accumulated mercury. As anode we used a saturated calomel electrode, connected to the electrolyzer by a salt bridge of agar-agar and potassium chloride solution.

The experiments were run as follows. The dry electrolyzer was first filled with pure nitrogen, and then some mercury was introduced into it. The surface of the mercury in the electrolyzer was covered with 1 to 2 drops of trichloroethylene in order to protect the mercury from oxidation. A current of pure nitrogen was first passed through the investigated solution for 20 minutes. Using a microburette, exactly 0.5 ml of the investigated solution (stypticine in suitable buffer solution) was introduced into the electrolyzer. By means of a ratchet device the capillary end of the dropping electrode was immersed in the investigated solution. Then a polarization voltage of −1.3 v was applied, and the height of the diffusion current was recorded. The value of the residual current was established from a previous experiment with the buffer solution, on which ground the polarographing was run (in the proper interval of voltages). Changes in the height of the diffusion current were recorded at 10 minute intervals. The obtained readings were plotted on the graph "time—current," and the points falling on a straight line were taken for subsequent calculations. The polarographing was run for 50 minutes, the same as in the experiments of Stromberg and Markacheva [5] and of Reynolds and Shalgosky [6].

For the work we used a SGM-8 polarograph and a M21/5 magnetoelectric galvanometer. The galvanometer was previously calibrated.

The polarographic coulometry of stypticine gave the following data. The initial concentration c_0 of stypticine was equal to 2890 μg in 1 ml, or 11.3 mmoles/liter. The initial limiting current I_0 = 249.53 μ amps, from which

$$I_0/c_0 = 249.53 : 11.3 = 22.08$$

The data for calculating according to formulas (1) and (2), both by the logarithmic and by the arithmetical method and the relationship between the limiting current and the time are given in the Table.

From the obtained data it follows that two electrons participate in the reduction of stypticine at a dropping mercury electrode. Taking into consideration the structure of stypticine, it can be assumed that this reaction goes due to involvement of the double bond of the heterocyclic ring. The presence of one wave indicates that the reduction is apparently single-stage. A two-electron wave in the reduction of stypticine (cotarnine) was also established by Coufalik and Santavy [8] using the spectrographic method.

Data for Calculating the Number of Electrons Involved in the Reduction of Stypticine at a Dropping-Mercury Electrode

Time (sec)	Diffusion current		Logarithmic method of calculation		Arithmetical mean method of calculation	
	(mm)	(μA)	$K = \frac{t}{\lg \frac{h_0}{h_t}}$	n (number of electrons)	$\frac{h_0+h_t}{h_0-h_t}$	n (number of electrons)
0	222	249.5	—	—	—	—
600	174	195.5	5668	1.13	8.25	1.13
1200	160	179.9	8427	1.68	6.16	1.69
1800	156	175.3	11749	2.34	5.72	2.35
2400	139	156.2	11805	2.35	4.35	2.39
3000	126	141.6	12369	2.46	3.62	2.43
			Average	1.992		1.998

SUMMARY

1. Using the method of polarographic coulometry it was established that two electrons are involved in the reduction of stypticine at a dropping-mercury electrode.

2. Taking into consideration the structure of stypticine, it can be assumed that this reaction goes due to involvement of the double bond in the heterocyclic ring.

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Received January 18, 1957

THE PREPARATION AND CERTAIN PROPERTIES OF SILICON NITRIDE

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The literature reports the presence in the silicon—nitrogen system of three chemical compounds: Si_3N_4, Si_2N_3 and SiN [1]; the only nitride whose existence has been definitely established, however, is Si_3N_4, which contains 39.8% nitrogen. According to the data in [2], obtained by x-ray and electron diffraction analysis, Si_3N_4 has a rhombic lattice (isomorphous with Ge_3N_4) with spacings $a = 13.38 \pm 0.03$, $b = 8.60 \pm 0.2$, $c = 7.74 \pm$ ± 0.02A. The sp. gr. of the compound Si_3N_4 according to various data is equal to 3.17-3.44 g/cc [3], m. p. 1900°. The nitride is exceptionally stable chemically. Thus the following reagents had no effect upon it in tests of 500 hours duration: HCl, H_2SO_4, HNO_3, H_3PO_4 at all concentrations, chlorine (at 900°), H_2S (at 1000°), boiling 25% NaOH solution. Molten NaOH dissolves Si_3N_4. The nitride is decomposed by hydrofluoric acid solutions. Silicon nitride is very resistant to the action of molten metals: aluminum at 1000° (shows no decomposition after 100 hours), lead at 400° (144 hours), tin at 300° (144 hours), zinc at 550° (500 hours), magnesium at 750° (20 hours); the nitride is corroded appreciably in contact with molten copper [3].

The stability toward oxidation in air, expressed as the increase in weight on unit surface after oxidation for 2 hours, is 5.0 mg/cm^2 for Si_3N_4, compared with, for example, 10.0 mg/cm^2 for TiB_2 and 42.5 mg/cm^2 for hot-pressed titanium carbide.

A number of methods have been proposed for the preparation of silicon nitride: direct combination of elemental silicon with nitrogen [1, 4], heating a mixture of silica and carbon in a current of nitrogen [1], heating silicon carbonitride in a current of nitrogen [5], ignition of triimidodisilene [1] and a number of others [6, 8].

In the present work the preparation of Si_3N_4 was checked using two of the methods given in the literature — by nitriding a mixture of silica and carbon and by the direct nitriding of elemental silicon. Certain properties of this compound have also been studied.

Nitriding a Mixture of Silica and Carbon

The composition of the charge was calculated from the equation $3SiO_2 + 6C + 2N_2 = Si_3N_4 + 6CO$. The charge was prepared by mixing SiO_2 and finely divided carbon in steel drums for 6 hours and afterwards sifting 3 times through a coarse sieve (20 mesh). The charge was heated in small graphite boats in a graphite tube furnace to 1000-1800°, the temperature being maintained constant for one hour every 100°.

It was established by chemical analysis of the specimens that at all temperatures the predominant reaction is the formation of silicon carbide, whose concentration in the products of the nitriding process amounts to 15% at 1400° and up to 85% at 1800°; the concentration of nitrogen does not exceed $0.5 \div 1.5\%$, i.e., the yield of Si_3N_4 is equal to 2-4%.

Nitriding Silicon Powder

The reaction was carried out in a TVV-2 furnace with tungsten heater, using elemental silicon powder of 99.92% purity (the particle size did not exceed 40 μ). The nitrogen was first purified from oxygen and moisture by the usual method — a 2-fold passage through a column of copper turnings at 540° and a 2-fold dehydration with phosphorus pentoxide. The nitrogen was not analyzed after it had been thus purified; the agreement between the sum of the concentrations of Si + N and 100% in the specimens obtained in the nitriding process, however, indicates that it was sufficiently pure. Twenty g samples of the silicon powder were placed

TABLE 1

Nitriding Silicon Powder

Temperature		$\frac{1}{T} \cdot 10^3$	N concentration (%)	Phase composition	Lattice spacing (A)				Reaction constant K (g/cc · · sec.)	log K
°C	°K				Si-phase	Si_3N_4-phase				
					a	*a*	*b*	*c*		
742	1015	0.988	0	Si	5.41_8		—	—	—	—
826	1099	0.914	0	Si	5.41_7	—	—	—	—	—
910	1183	0.846	0	Si	5.41_9	—	—	—	—	—
970	1243	0.805	0.29	$Si + Si_3N_4$	5.41_9	—	—	—	$7.49 \cdot 10^{-7}$	−6.1255
1004	1277	0.785	6.45	$Si + Si_3N_4$	5.41_9	—	—	—	$2.94 \cdot 10^{-6}$	−5.5317
1130	1403	0.712	15.94	$Si + Si_3N_4$	5.41_8	13.37_5	8.59_8	7.74_3	$1.88 \cdot 10^{-5}$	−4.7258
1216	1459	0.672	26.35	$Si + Si_3N_4$	5.41_4	13.38	8.60_0	7.74_5	$4.15 \cdot 10^{-5}$	−4.3820
1400	1673	0.597	37.31	$Si + Si_3N_4$	5.41_9	13.38_2	8.59	7.74_4	$9.61 \cdot 10^{-5}$	−4.0173
1490	1763	0.568	38.32	$Si + Si_3N_4$	5.41_8	13.37_9	8.59_9	7.74_1	$2.00 \cdot 10^{-4}$	−3.6990
1600	1873	0.536	39.71	$Si + Si_3N_4$	5.41_9	13.38_3	8.59_7	7.74_1	$3.32 \cdot 10^{-4}$	−3.4789

in corundum crucibles. With a constant pressure of nitrogen of 1 atmosphere, the temperature was raised to the required value in 10 minutes, after which this temperature was maintained for 0.5-20 hours until the silicon had been completely saturated with nitrogen at the required temperature. The appropriate data for several temperatures are given in Fig. 1.

It should be noted that the corundum crucibles do not react at all with the silicon, since in the very first moments of the action of the nitrogen on the silicon powder, each particle becomes covered with a compact film of refractory nitride, and further transfer of the nitrogen to the silicon is brought about by a diffusion process (transmission diffusion through the layer.) Thus from the very beginning of the nitriding process, in the 10-minute interval in which the temperature is being raised, the silicon is enveloped in a refractory covering of silicon nitride which does not react with the Al_2O_3 or other material in the crucibles up to high temperatures.

The temperatures in the furnace during the experiments were measured up to 1300° using a platinum platinorhodium thermocouple, and above this temperature using an optical pyrometer graduated by means of the platinum platinorhodium thermocouple under conditions corresponding to the working conditions, which made it necessary to introduce corrections for the absorption of the medium, the quartz window, etc.

The technical experiments carried out on the saturation of silicon powder with nitrogen were not undertaken for the purpose of making a complete study of the equilibrium and kinetics of the nitriding reaction $3Si + 2N_2 \rightleftharpoons Si_3N_4$; they may, however, give approximate values for the constant for this reaction and for the energy of activation for the diffusion formation of the nitride phase Si_3N_4, which was identified in all the specimens from 970° onward by x-ray structural examination. This was carried out by photographing the specimens, obtained during the nitriding process, in a camera of 85.78 mm diameter using Cu Kα-radiation with a Ni filter and an exposure of 10-12 hours. The x-ray diffraction patterns for Si_3N_4 are very complex and contain approximately 110 lines. The most intense lines, with $\underline{d}$ equal to 0.9497, 0.9515, 0.9620, 0.9710 and 0.9827, were chosen for the calculation of the lattice spacing.

From the data obtained, which are given in Table 1, we may reach the preliminary conclusion that nitrogen has either no solubility, or very slight solubility, in silicon, and that there is no appreciable range of homogeneity of the Si_3N_4 phase. It should be noted that the x-ray diffraction patterns showed no other

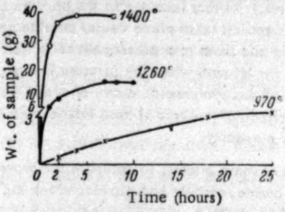

Fig. 1. Curves showing the saturation of silicon with nitrogen.

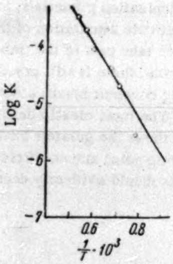

Fig. 2. The relationship between the logarithm of the nitriding reaction constant and the temperature.

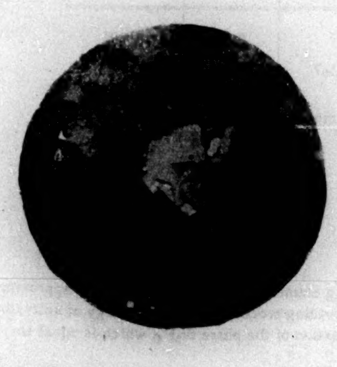

Fig. 3. Photomicrograph of nitrided area in silicon powder (×660).

phases than Si and Si_3N_4, which renders doubtful the existence of the phases SiN and Si_2N_3 reported in the literature. The "SiN phase" may be taken from the results of chemical analysis of the mixture Si + Si_3N_4; as regards the "Si_2N_3 phase," it is difficult to account for its detection in certain older works.

From the data giving the increase in weight during the absorption of nitrogen, using the method adopted by Gulbransen and his school [7], we calculated approximate values for the nitriding reaction constant,

$$K = \frac{\Delta p}{v\tau}$$

where: Δp – increase in weight in the nitriding process (g), $\underline{v}$ – volume of silicon before the nitriding process (cc), τ – saturation time at constant temperature (seconds.)

The numerical values for the reaction constant, calculated according to the formula, are given in Table 1 and have been used to construct the curve given in Fig. 2.

It should be noted that the nitriding process at temperatures above 1600° gives lower increases in weight, while at 1820° there is no increase in weight at all. This cannot be explained by volatilization of the silicon, since the silicon particles, as pointed out above, are covered with a refractive layer of Si_3N_4. This last circumstance also apparently explains the fact that a change in the state of aggregation of the silicon at 1423° has no appreciable influence on the rate of reaction. It must therefore be assumed that at temperatures above 1600°, either Si_3N_4 is not formed at all or else its rate of dissociation is greater than its rate of formation. From this it may be concluded that the dissociation pressure of Si_3N_4, given in the literature as equal to 1 atmosphere at 1977°, is somewhat low; a dissociation pressure equal to 1 atmosphere is reached at a temperature of the order of 1780-1820°.

The energy of activation for the diffusion of nitrogen into silicon with the formation of the phase Si_3N_4 has been calculated from the values of the reaction constant for the nitriding process and found to be equal to 33800 ± 719 cal/mole.

The nitride formed in the nitriding process has a well-defined crystalline structure (Fig. 3) with a particle size of 10-15 μ; the microhardness of the Si_3N_4 crystals (determined using a PMT-3 apparatus with an indenter load of 60 g) is equal to 3337 ± 120 kg/mm^2. The microhardness of the inclusions of the silicon phase is equal to approximately 900 kg/mm^2. It is practically equal to the hardness of the original silicon powder, which provides confirmation that nitrogen is insoluble or only very slightly soluble in silicon.

Compression of silicon nitride powder at pressures as low as 6 tons/cm² leads to the formation of stable briquets with a density of 2.72-2.74 g/cc (i.e., with 20-25% of pores.) Further increase in the pressure at which compression takes place causes considerable internal stress and leads to a consequent reduction in the density of the briquets when the pressure is removed. The shape of the compression curve obtained (Fig. 4) is characteristic of powders of hard brittle materials with a low plasticity.

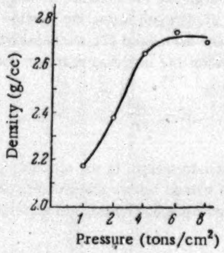

Fig. 4. The relationship between the density of silicon nitride briquets and the pressure used for compression.

It is of some interest to compare the properties of silicon boride, carbide and nitride, which are given in Table 2 [3, 4, 8].

Without taking into account the influence of the difference in the crystal structures, it may be suggested that in the series Si—B, Si—C and Si—N there is a change in the nature of the bond between the silicon and the metalloid from metallic to covalent. Boron and silicon, which have similar ionization potentials, undoubtedly form a common electronic association of the weakly-bound electrons which take part in the transfer of current. In silicon carbide, there is still preserved, in addition to the strong covalent bonds, a bond of the metallic type, which is responsible for the fairly low electrical resistance. The most clearly defined compound of the type with covalent bonds is silicon nitride, which in this series shows the greatest brittleness (with the lowest hardness) and electrical resistance, together with the lowest melting point and coefficient of thermal expansion. The activation energy of the formation by diffusion of the phases should evidently decrease in the order Si—N, Si—C and Si—B.

TABLE 2

A Comparison of the Properties of Silicon Boride, Carbide and Nitride

Property	SiB_3	SiC	Si_3N_4
Melting point (or dissociation temperature) (°C)	2750°	2600°	1900°
Microhardness in kg/mm² (with	5352 ± 167	3340	3337 ± 120
Modulus of elasticity (kg/mm²)	—	2900—4700	11600—14500
Specific resistance (in Ω · cm)	Good conductor of electricity	50	$1.426 \cdot 10^3$
Coefficient of thermal expansion	—	$4.86 \cdot 10^{-6}$	$2.75 \cdot 10^{-6}$

SUMMARY

1. A study has been made of the conditions for nitriding elemental silicon at 970-1600°. Approximate values have been obtained for the reaction constant for the nitriding process and for the energy of activation of the reactive diffusion of nitrogen into silicon with the formation of the phase Si_3N_4, which is equal to 33800 ± 719 cal/mole.

2. The microhardness of Si_3N_4 has been determined and found to be equal to 3337 ± 120 kg/mm²; it has been established that the solubility of nitrogen in silicon is small and that there is no range of homogeneity of the phase Si_3N_4.

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Received December 21, 1956

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THE ELECTROLYTIC REDUCTION OF THORIUM TETRACHLORIDE IN SALT MELTS

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Until recently it was considered that thorium could only have a valence of four in its compounds. In connection with the problem of the placing of the actinide elements in the periodic system of the elements, studies have been made on the preparation of thorium compounds of lower valence. In the literature of recent years there are reports [1-3] that at increased temperatures (of the order of 500-600°), either by synthesis from the elements, or by the reaction between the metal and the tetrahalide, it has been possible to prepare halogen derivatives of di- and trivalent thorium. The lower compounds of thorium are very reactive. They exhibit powerful reducing properties; they react with the glass walls of containing vessels, forming compounds of the type $ThOX_2$; and they react with water with the formation of Th^{4+} and evolution of hydrogen.

At temperatures above 600° the lower halogen derivatives of thorium decompose according to the equations:

$$2ThX_3 \rightarrow ThX_4 + ThX_2$$
$$2ThX_2 \rightarrow ThX_4 + Th.$$

It has been shown by work in our laboratory that metallic thorium in salt melts reduces Th^{4+} ions to lower valence states. The reduction stops at the stage of Th^{2+} formation. The lower chlorides, being dissolved in the melt, are not decomposed to an appreciable extent even at a temperature of the order of 900°.

In one of our previous works [4] on the study of cathodic processes in the electrolysis of chloride melts containing Th^{4+} ions, it was established that lower chlorides of thorium are intermediate products in the electrolytic preparation of the metal. As laboratory experiments show, thorium, during the electrolysis, does not begin to be deposited immediately, but only after a certain "critical" value for the cathodic current density has been reached. At current densities lower than this limiting value the process taking place involves only a change in the charge of the Th^{4+} ions to Th^{2+} and Th^{3+}.

It is thus possible to prepare lower chlorides of thorium by an electrochemical method in salt melts by electrolysis at low current densities.

It has proved of interest to make a more detailed study of the conditions for the electrochemical reduction of thorium in salt melts and, in particular, to study the properties of an electrolyte containing an appreciable quantity of lower valence thorium ions.

Melts containing Th^{2+} and Th^{3+} exhibit powerful reducing properties. Considerable difficulties in this connection had to be overcome in the search for a suitable material for the preparation of the cell and the creation of an inert atmosphere.

The materials usually employed for the preparation of electrolytic cells – glass, quartz, porcelain and even alundum – proved to be unsuitable for our experiments. The relatively small quantities of Th^{3+} and Th^{2+} ions which enter the melt during the electrolysis are very rapidly lost as a result of reaction with the material of the cells walls.

It can be shown on the basis of existing thermodynamic data that Th^{2+} will reduce aluminum oxide at the temperature of the experiment (700°): $2Al_2O_3 + 6ThCl_2 \rightleftharpoons 4Al + 3ThO_2 + 3ThCl_4$, the change in the isobaric potential for this reaction being

$$\Delta Z = 49.100 - 118.2T \text{ cal/mole}$$

from which

$$\Delta Z \leq 0 \quad \text{at} \quad T \geq 500°.$$

This reaction, however, could not be materially reflected in the previous studies on the reduction of the tetrachloride by metallic thorium in melts, since a fairly massive piece of metallic thorium was taken for the experiments and the process by which the thorium entered the melt according to the reaction:

$$Th^{4+} + Th \rightarrow 2Th^{2+}$$

compensated for the slower removal of Th^{2+} ions from the melt as a result of their reaction with the walls of the cell.

We also tested several metals as materials for the preparation of a cell. Pt and Ta gave unsatisfactory results. Crucibles prepared from these metals gave a considerable loss in weight after electrolysis and were extensively destroyed on their surfaces. In this case, in all probability, interaction leads to the formation of alloys of thorium and the corresponding metal.

The most suitable material for the preparation of the crucible in which the electrolysis was carried out proved to be metallic molybdenum. Its surface after the electrolysis showed no visible alteration, and the weight remained constant. All the experiments on the study of the electrolytic reduction of $ThCl_4$ in salt melts were therefore carried out in molybdenum crucibles.

The lower chlorides of thorium are very sensitive even to traces of oxygen. The argon with which the cell was filled was therefore carefully purified. For this purpose the gas was passed in turn through a tube filled with calcium (500°), then through turnings of metallic magnesium (450°), and finally through a tube containing metallic titanium in a furnace (500°). As a measure of the purity of the gas it was observed that after the electrolysis, which lasted for a considerable time (5-6 hours), the surface of the molybdenum crucible had undergone no visible change. The crucible did not lose its characteristic metallic luster.

The construction of the cell in which the studies were carried out is represented diagramatically in Fig. 1. The melt containing the thorium tetrachloride was placed in the molybdenum crucible, which also served as the cathode. A hollow carbon tube was used as the anode. In order to prevent the chlorine liberated at the anode from entering the electrolyte containing the reduced species, the anode region was separated from the cathode region by an asbestos diaphragm. At the same time the anode was placed in a separate quartz tube, into the foot of which was sealed a capillary packed with asbestos.

The electrolysis for the preparation of the lower chlorides of thorium was carried out at a temperature of 700° in a melt of alkali metal chlorides containing 16.1% by weight of $ThCl_4$. The current density was of the order of 0.001-0.008 amp/cm^2. The time of electrolysis depended on the value of the current density.

Results and Discussion

As the reduced species accumulate, the melt becomes darker and darker, the lower chlorides of thorium giving it a grey coloration. If such a melt, containing an appreciable amount of the chlorides of di- and trivalent thorium, is brought into contact with air, oxidation takes place very violently with flashes of combustion, the whole melt sparkles and crackling noise is heard.

In order to confirm the reducing properties of the melt containing the lower chlorides of thorium qualitatively, it was cooled in an inert atmosphere, after which the solid ash-like mixture was treated with $FeCl_3$ and the presence of the reduced species established by back-titration with a dilute solution of $K_2Cr_2O_7$. Since oxygen, dissolved in the water, is introduced with the $FeCl_3$ solution, no definite conclusions can be reached concerning the quantitative relationships.

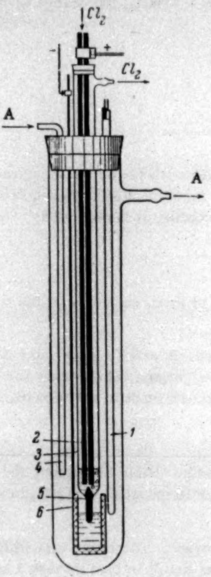

Fig. 1. The cell. 1) Thermocouple, 2) carbon anode, 3) quartz tube, 4) tube for passing in the argon, 5) asbestos diaphragm, 6) molybdenum crucible with current lead (cathode).

In order to estimate the quantitative changes taking place in the melt during the electrolysis, we measured the oxidation-reduction potentials of the system. The potential of an inert molybdenum electrode (the cathode) was recorded every 10-15 minutes using an oscillograph. The anode was used as reference electrode. At the moment when the potential was being measured, the electrolysis circuit was broken. In order to ensure that there was no change in the potential of the reference electrode at the moment when the circuit was broken, additional chlorine, prepared by the electrolysis of lead chloride, was bubbled through it.

As the measurements showed, the potential of the inert electrode during the course of the electrolysis changes according to the equation:

$$E = E_0 + \frac{RT}{2F} \ln \frac{a_{\mathrm{Th}^{4+}}}{a_{\mathrm{Th}^{2+}}},$$

where $a\mathrm{Th}^{4+}$ and $a\mathrm{Th}^{2+}$ = the activities of the Th^{4+} and Th^{2+} ions. In our experiments the concentrations of the ions may be used in the equation instead of the activities, since studies in our laboratory have shown [5] that melts containing less then 25% by weight of $\mathrm{ThCl_4}$ behave as ideal solutions.

The values obtained were used to construct curves showing the change in the oxidation-reduction potential of the $\mathrm{Th}^{4+}/\mathrm{Th}^{2+}$ system with time (with $\underline{i}$ = constant.) The measurements were carried out for three values of the current strength: 0.01, 0.05 and 0.1 amp. Figure 2 shows the corresponding curves. Examination of the curves reveals the presence of a number of characteristic regions. This in all probability indicates the stepwise nature of the process of reduction of the Th^{4+} ions.

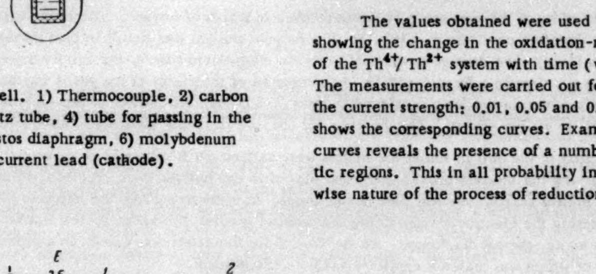

Fig. 2. Polarization of an inert electrode (the cathode) in a molten equimolar mixture of potassium and sodium chlorides containing 16.1% by weight of $\mathrm{ThCl_4}$ at 700°. Current strength (in amp.) 1) 0.1, 2) 0.05, 3) 0.01.

Taking account of the fact that the reduction at the cathode takes place with 100% yield, it is possible to calculate the quantity of electricity which must be passed in order to reduce all the Th^{4+} ions present in the melt to the di- or trivalent state, and then to metallic thorium. As the calculations show, the quantity of electricity required theoretically for the reduction of the Th^{4+} to the lower valence states is close to the values obtained in practice.

SUMMARY

1. A study has been made of the electrolytic reduction of thorium tetrachloride at the cathode in melts of alkali metal chlorides containing 16.1% by weight of $ThCl_4$ at 700°.

2. It has been established that thorium, in its lower valence states, reacts vigorously not only with silicate materials (quartz, glass, porcelain, alundum), but also with a number of metals (Pt and Ta), as a result of the formation of the corresponding alloys with thorium.

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Received December 27, 1956

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*Original Russian pagination. See C. B. Translation.

ELECTROLYTIC DISSOCIATION IN NONAQUEOUS SYSTEMS

VI. SYSTEM ALLYL MUSTARD OIL—o-TOLUIDINE

S. P. Miskidzh'ian

As is known, the reaction of allyl mustard oil with amines yields substituted thioureas [1], which are not electrolytes. On the other hand, it was shown that systems, prepared from allyl mustard oil and an aromatic amine (aniline, o-toluidine, etc.), are good conductors of an electric current. The specific electroconductivity of such systems reaches the order of $10^{-3}\Omega^{-1}cm^{-1}$ [2, 3]. It is difficult to explain the presence of a high electroconductivity if it is assumed, in accord with general opinion, that the reaction products of allyl mustard oil with amines are simply substituted thioureas.

In a number of papers published by us [4, 5] it has been shown that in such systems, together with the formation of the substituted thiourea, the allyl-amine thiocyanate is also obtained; this is an electrolyte and responsible for the high electroconductivity shown by the solutions. In the indicated papers we have given the mechanism for the electrolytic dissociation of these compounds, the anion of which in all cases is SCN^-. In this paper we communicate the results obtained in studying the system allyl mustard oil—o-toluidine.

The fusion, viscosity, density, surface tension and electroconductivity properties of this system have been studied by N. A. Trifonov, K. I. Samarina and co-workers [2]. The diagrams for all of these properties show a singular point and clearly indicate that the components of this system react vigorously with each other to yield allyl-o-tolylthiourea. According to the data of the authors mentioned, the specific electroconductivity isotherm has two maxima and one minimum, found at 50 mole %, i.e., corresponding to the composition of this compound.

The maximum specific conductivity κ_{80} reaches a volume of $1.69 \cdot 10^{-3}$. Neither allyl mustard oil, nor o-toluidine, nor (especially) allyl-o-tolythiourea, the latter being the main reaction product of the indicated components, are electrolytes nor can they create such a high electroconductivity in the system. It would be natural to assume here the allyl-o-toluidine thiocyanate, which is an electrolyte and determines the comparatively high electroconductivity shown by the solution, is formed, together with substituted thiourea, as in the systems studied earlier by us.

It is our opinion that an investigation of similar systems could possess some practical value, since the allyl-amine thiocyanates are salts of ammonium bases, which in recent years are widely used in medicine as bactericidal and ganglion-blocking agents.

EXPERIMENTAL

Allyl mustard oil was obtained by the earlier described method [4]. The o-toluidine after long standing over potassium hydroxide was distilled, and for our work we took the fraction with b. p. 196-197° (746 mm), d_{20} 0.9990, n_D^{20} 1.5735. The prepared mixtures were kept in sealed ampoules in the dark. Despite, this most of the mixtures turned brown on long standing (about 1 year). The mixtures containing from 30 to 60 mole % o-toluidine solidified completely, while the mixtures containing 20, 70 and 80 mole % o-toluidine showed a crystalline precipitate after several days.

As was true of systems we studied earlier, all of the solutions of the present system showed the presence of SCN^- ion by the usual qualitative tests ($FeCl_3$, etc.).

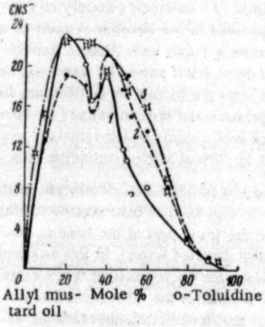

Fig. 1. Relationship between the SCN^- concentration (in weight % on the compound having SCN^- as the anion) and the composition of the mixtures of the system. 1) When the mixtures were stored for 13 months, 2 and 3) after the mixtures were heated for 28 and for 94 hours.

In this connection we decided to determine the SCN^- concentration as a function of the composition of the system. A photoelectrocolorimeter was used as the measuring device (for a detailed description of the method see [5]). The relationship between the SCN^- concentration (in weight % on the compound having SCN^- as the anion) and the composition of the mixtures, which were stored for 13 months, is shown in Fig. 1.

Earlier in studying similar systems we had observed that heating the mixtures leads to increasing the SCN^- concentration in them. For this reason we subjected all of the solutions of the present system to prolonged heating in a thermostat at 100 ± 5°. The relationships between the SCN^- concentration and the composition when the heating time was 28 and 94 hours are also shown in Fig. 1.

According to the data of [2], the mixture containing 80 mole % allyl mustard oil shows an extremely high electroconductivity. As is not difficult to see, on the SCN^- concentration—composition diagram the maximum SCN^- concentration corresponds to this composition. This fact and some other experimental data, which will be discussed below, make it possible to assume that also in the given system the reaction of allyl mustard oil with o-toluidine gives, parallel with the formation of allyl-o-tolylthiourea, a certain amount of allyl-o-toluidine thiocyanate according to the reaction $CH_3C_6H_4NH_2 + CH_2 = CHCH_2NCS \rightleftharpoons [CH_3C_6H_4\overset{+}{N}H_2CH_2CH{=}CH_2][SC\overline{N}]$. This last substance is an electrolyte; in its own medium, and also with an excess of the components present, it dissociates into ions.

As can be seen from Fig. 1, the amount of allyl-o-toluidine thiocyanate in some of the mixtures reaches 22.8%, which shows that the side reaction reaches substantial proportions in the indicated mixtures. A long heating of the mixtures does not lead to a substantial increase in the SCN^- concentration, as was observed in the systems studied by us earlier [5]. A possible explanation for this is the fact that, in contrast to the previous systems, we measured the SCN^- concentration in the present system some time (more than a year) after the preparation of the mixtures, i.e., after the reaction for the formation of allyl-o-toluidine thiocyanate was practically complete.

In studying the system allyl mustard oil—aniline [5] we were able to show that the allylphenylthiourea formed in the system is converted to allyl-aniline thiocyanate on long heating. To determine if a similar transformation also occurred in the present system, we prepared a mixture containing 50 mole % allyl mustard oil and 50 mole % o-toluidine. This mixture turned completely solid after several days, forming mainly allyl-o-tolylthiourea and a small amount of allyl-o-toluidine thiocyanate. The latter substance is responsible for the substantial electroconductivity (according to our measurements $\kappa_{70} = 2.8 \times 10^{-4}$) and brown color shown by the mixture. After repeated washing with ethyl alcohol of the solidified mixture obtained by us, followed by recrystallization, we obtained the pure allyl-o-tolylthiourea as a colorless crystalline substance with m. p. 92° and $\kappa_{100} = 2.7 \times 10^{-6}\ \Omega^{-1}\ cm^{-1}$. The allyl-o-tolylthiourea obtained in this manner was then heated for a long time in a sealed ampoule (for 10 days) at 100 ± 5°. After this length of heating the mixture was shown to contain up to 8.5% of allyl-o-toluidine thiocyanate.

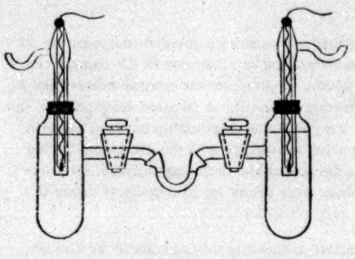

Fig. 2. Electrolysis apparatus. Explanation in the text.

To isolate the allyl-o-toluidine thiocyanate from the prepared mixtures we made use of the fact that it is readily soluble in hot water. Therefore, the compound in which we were interested was extracted with hot water until the aqueous extract failed to give a positive test for SCN^- ion. After extraction, a certain amount of tarry substance remained on the bottom of the extraction flask. A cloudiness (mainly allyl-o-tolylthiourea) appeared in the aqueous extracts on cooling. After the water extracts were filtered through several layers of dense filter paper the water was completely removed from the filtrate by distillation, first at atmospheric pressure and then in vacuo (10-20 mm). Here a very thick brown liquid which remained in the flask contained 70-73% of allyl-o-toluidine thiocyanate.

This liquid was subjected to electrolysis in the apparatus shown in Fig. 2. The investigated substance was contained in the lower part of the bend in the U-shaped tube. All of the remaining volume of the apparatus was filled with distilled water. In this way both the anodic and cathodic areas contain nothing else but water, which eliminates the progress of side electrochemical processes at the electrodes during the passage of a current and simplifies the subsequent analysis of the anolyte and catholyte. With such a construction of the apparatus the transfer of substances into the anodic and cathodic areas due to diffusion is excluded, or at least reduced to a minimum. The electrolysis was conducted at a voltage of 400-500 v. Here the current (intensity) at the start of experiment did not exceed 0.2-0.5 milliamp, but then it gradually rose and at the end of experiment reached 10 milliamps.

During electrolysis the SCN^- ions migrate to the anode, which is confirmed by the test with $FeCl_3$. Neutralization of the anolyte with KOH solution, followed by evaporation, left a crystalline substance which proved to be potassium thiocyanate.

Evaporation of the catholyte in vacuo (10-20 mm) left a viscous brown liquid. When dissolved in water this liquid showed strongly alkaline.

The experiments made with the electrolyzer support the formation of allyl-o-toluidine thiocyanate when allyl-o-tolylthiourea is heated, and its dissociation into the ions SCN^- and $[CH_3C_6H_4NH_2CH_2CH{=}CH_2]^+$.

SUMMARY

1. It was shown that the reaction of allyl mustard oil with o-toluidine yields, together with allyl-o-tolylthiourea, allyl-o-toluidine thiocyanate.

2. The abnormally high specific electroconductivity shown by the system allyl mustard oil—o-toluidine is due to the formation of the allyl-o-toluidine thiocyanate.

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Received December 10, 1956

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*Original Russian pagination. See C. B. Translation.

LETTER TO THE EDITOR

ENTHALPY OF FORMATION OF NICKEL CARBONYL

B. F. Ormont and E. I. Smagina

In 1955 we published a paper [1] in which the enthalpy of formation of liquid nickel carbonyl was determined by the explosion method developed by us. As had been shown by us ([1], page 229), for the reaction $[Ni]_\beta + 4CO = Ni(CO)_4$ (liquid), $\Delta H^0_{f,298} = -47.3 \pm 1$ kcal/mole. The use of this method permitted making some important corrections in the earlier found values for the enthalpy of formation of this carbonyl.

In a paper [2] that was published at the same time as ours, two values were given for the enthalpy of formation of gaseous nickel carbonyl: $\Delta H^0_{f,298} = -36.3$ kcal/mole (indirect determination) and $\Delta H^0_{f,298} = -34.5$ kcal/mole (direct determination).

In order to compare the results given in these two papers it is necessary to take into account the value of the enthalpy of vaporization of nickel carbonyl, which in the studies of various authors varies from 6.3 to 7.2 kcal/mole [2, 3]. In reference [2] the value $\Delta H^0 = 6.5$ kcal/mole is assumed to be the most probable, taken from an old study [4]. If we proceed from later studies, where $\Delta H^0 = 6.92$ [5] and $\Delta H^0 = 7.2$ [3], then the value of ΔH^0 should be taken equal to 7.0 kcal/mole.

Next, in order to compare the values for the enthalpy of formation of nickel carbonyl, computed from the experimental values of the heats of combustion, it is necessary to operate with the same values for the enthalpies of formation of the components, entering into the equation of the reaction. But in the case of NiO some differences exist in the literature on this score. Thus, in [6] the value $\Delta H^0_{f,298} = -59.3$ kcal/mole is assumed, and in [7] the value $\Delta H^0_{f,298} = -57.3$ kcal/mole. In our paper [1] a value of -58.9 kcal/mole was assumed, and in reference [2] a value of -57.3 kcal/mole. Some critical remarks concerning study [7] were made by one of us in paper [8]. At the same time, previous determinations of this value are no more correct. Substituting in the equation ([1], page 229) the value -57.3 instead of -58.9, which is completely obligatory when the results of the two studies are compared, we obtain an average correction for the value of $\Delta H^0_{f,298}$ for $Ni(CO)_4$ (liquid), found in [1] to be equal to 1.2 kcal/mole, i.e., $\Delta H^0_{f,298} = -47.3 + 1.2 = -46.1$.

As a result, the enthalpy of formation of gaseous nickel carbonyl, computed from the enthalpy of formation of the liquid carbonyl, found in [1], is equal to $\Delta H^0_{f,298} = -47.3 + 6.5 + 1.2 = -39.6$ kcal/mole, i.e., it is 5.1 kcal/mole greater than the value found by direct determination by the British authors in [2]. If for the enthalpy of vaporization of the carbonyl we assume a value of 7.0 kcal/mole (see above), then from our data for the liquid carbonyl we obtain for the enthalpy of formation of the gaseous carbonyl $\Delta H^0_{f,298} = -39.1$ kcal/mole. This last value had already been communicated by one of us [9].

A publication by some American authors [10] appeared recently, in which the value for the enthalpy of formation of gaseous nickel carbonyl is given equal to $\Delta H^0_{f,298} = -39.1$ kcal/mole (± 0.5 kcal).*

Since in [10] for the calculations a value of 6.5 kcal/mole was taken for the enthalpy of vaporization of the carbonyl, and a value of -57.3 kcal/mole for the enthalpy of formation of NiO, then the value of -39.1 kcal/mole found in [10] corresponds to the value of -39.6 kcal/mole found in our work. In other words, the results given by us in [1] for the determination of the enthalpy of formation fo the liquid carbonyl are fully supported by the value given in [10] for the enthalpy of formation of the gaseous carbonyl (within the accuracy limits of the determinations).

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* Considering the inaccurate value of the enthalpy of vaporization of the carbonyl, the accuracy indicated in [10] is high.

However in citing our data the authors of [10] permitted two gross errors: they fail to mention either that our calculation was made for the liquid carbonyl and theirs for the gaseous carbonyl, or that several different values for the enthalpy of formation of NiO were used in the calculations given in our paper. As a result of these peculiar errors the indicated authors do not compare the values −39.6 and −39.1, but instead the values −47.3 and −39.1, and they create some baseless assumptions that such a "difference" could be due to possible errors in our work.

We would like to emphasize here that our publication [1] does not give any grounds for these errors in [10]. On page 229 [1] it is clearly stated that the value of −47.3 kcal/mole for the enthalpy of formation relates to the liquid carbonyl: the equation given for the reaction bears the designation (l) after formula of the carbonyl. In the case of the gaseous carbonyl the designation would be (g). On the same page a calculation of the heat effect for the formation of the carbonyl is given three times using the value −58.9, and not −57.3 kcal/mole, for the enthalpy of formation of NiO.

In a later paper we propose to discuss some of the other erroneous assumptions expressed in [10].

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Received July 12, 1957

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*Original Russian pagination. See C. B. Translation.

A STUDY OF AQUEOUS SOLUTIONS OF ACETIC ACID BY THE METHOD OF RAMAN SPECTRA

A. A. Glagoleva and A. A. Ferkhmin

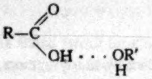
Some organic acids play a very important role in the living organism; however, their concentration in the latter is very small, and consequently their study encounters great difficulties. We decided to study the organic acids of greatest biological interest by the method of Raman spectra. The first acid taken by us for study was acetic acid as being the acid most studied by various methods. Despite this, many disputes have arisen regarding the change in the structure of acetic acid when the latter is diluted with water. Many different opinions also exist on the formation of hydrates.

Since previous investigations dealt mainly with high concentrations, we began our study with solutions of high concentration, gradually diluting them with water.

Most authors assume that acetic acid shows association into dimers [1-6]. Pauling and Brockway [7] showed that formic acid representsdimers in the form of closed rings. Huggins [8] expressed the theory that the dimers of monobasic acids are closed by two hydrogen bridges into a ring. Many assume that the ring dimers of monobasic acids suffer decomposition in polar solvents, like for example water, being converted on great dilution into monomers [9-12]. Some authors postulate that in liquid acetic acid, besides ring dimers, there is also present a certain amount of monomers and open dimers (for example, [6]). Huggins [8] indicates that liquid formic acid can, together with dimers, also form chain polymers composed of a large number of acid molecules. Batuev [13-15] postulates that the latter is also true for the acetic acid molecule.

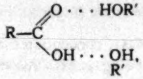
Contradictory opinions also exist on the possibility of forming hydrates in aqueous solutions of aliphatic acids. Jones [1] and Koteswaram [16] rejected the formation of hydrates. The majority of the authors [6, 8, 13-25] who studied these acids believe that hydrates are formed. Some authors indicate that dihydrates can also arise [6, 8, 19-24].

Recently a paper by Izmailov and Kutsyna [25] appeared, in which it is indicated that the behavior of carboxylic acids in solutions of monohydric alcohols is the same as it is in water. Two structures are given by them:



$\mathrm{R{-}C(=O){-}OH\cdots O(H)R'}$

and



$\mathrm{R{-}C(=O\cdots HOR'){-}OH\cdots O(H)R'}$,

corresponding to the mono- and dihydrate of the acid molecule in water.

In order to determine in more detail the behavior of acetic acid solutions in water, and mainly to study more dilute solutions, we investigated a large number of concentrations by the method of Raman spectra.

The microphotometric curves for various concentrations are shown in Figs. 1-3. The Raman spectra were taken using an ISP-51 spectrograph with a glass light filter, isolating the mercury line 436 mμ. An MF-2 microphotometer was used to obtain the microphotometric curves. An IZA-2 comparator was used to measure the frequencies. For convenience the microphotometric curves were divided into three parts; in Fig. 1, from 900 to 1900 cm^{-1}; in Fig. 3, from 150 to 1000 cm^{-1}; and in Fig. 4, from 2800 to 3750 cm^{-1}.

Passing over to a description of the microphotometric curves, we will first discuss the band most sensitive to a change in the concentration, namely, the band corresponding to the C=O bond (Fig. 1); this band also appears to be the most studied [5, 6, 10, 11, 14-17, 26-36].

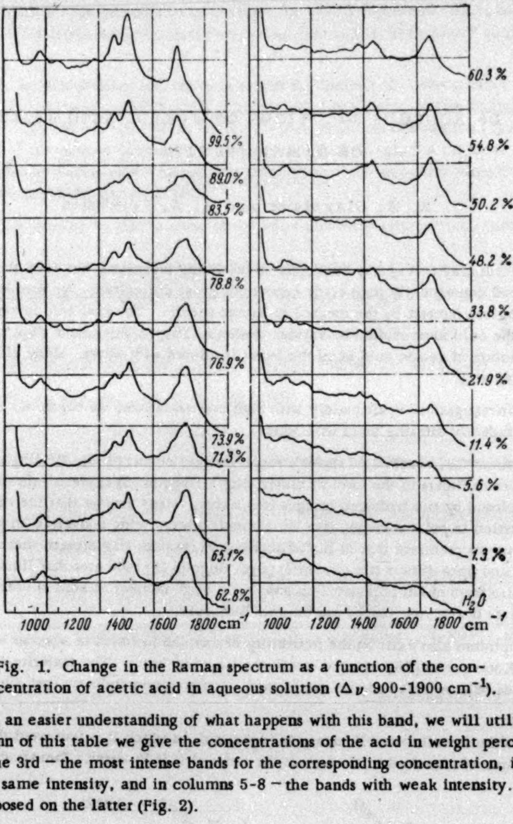
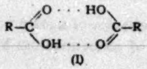


Fig. 1. Change in the Raman spectrum as a function of the concentration of acetic acid in aqueous solution ($\Delta\nu$ 900-1900 cm^{-1}).

In order to obtain an easier understanding of what happens with this band, we will utilize the table given below. In the 1st column of this table we give the concentrations of the acid in weight percent, in the 2nd column – in mole percent, in the 3rd – the most intense bands for the corresponding concentration, in the 4th – the bands with approximately the same intensity, and in columns 5-8 – the bands with weak intensity. The lines of the light source may be superimposed on the latter (Fig. 2).

According to the literature data, concentrated acetic acid shows bands at 1660 cm^{-1} (most intense), 1700-1710 and 1740 cm^{-1} (both of the latter being weak). As was shown by many authors, the band at 1660 cm^{-1} belongs to the ring dimer of type (I).



(I)

The presence of the 1700 and 1740 cm^{-1} lines suggests that open dimers [6] could also be present, but in small amount. Batuev [13] believes that these lines belong to higher polymers.

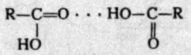
According to our investigations, in 99.5% acetic acid solution the band of the carbonyl group is relatively narrow, with a well-defined maximum at 1660 cm^{-1}; the remaining maxima of the band are weakly expressed (Fig. 1).

TABLE

Change in the Frequency of the C=O Group as a Function of the Concentration of Acetic Acid Solutions

Concentration (in wt. %)	Concentration (in mole %)	(in cm^{-1})					
1	2	3	4	5	6	7	8
99.5	1.66	1660	1700	1635			1755
89.0	1.48	1660	1700	1625			1740
83.5	1.39	1697	1665	1640			1745
78.8	1.31	1697	1690, 1667	1635			1745
76.9	1.28	1700	1687	1650. 1630			
73.9	1.23	1700		1650. 1620			1750
71.3	1.19	1700		1640			1750
65.1	1.08	1700	1680	1640			1760
62.8	1.05	1700	1690	1640			1755
60.3	1.00	1700	1690		1665		1750
54.8	0.91	1700	1690	1645. 1620	1675		1750
50.2	0.84	1700	1690	1640		1725	
48.2	0.80	1700	1690	1635			1745
33.8	0.56	1700		1645. 1625	1675		1740
21.9	0.36	1700	1695	1655			
11.4	0.19	1700		1630	1675		1765
5.6	0.09	1695	1705	1653. 1625		1720	1765
1.3	0.02	1695	1705	1652. 1620. 1640	1675	1725	1760. 1767
H_2O	—	—	—	1630	—	—	—

At 89.0% acid the 1660 cm^{-1} band continues to remain quite intense, but the maximum at 1700 cm^{-1} begins to get stronger. As a result of this the band becomes broader. It is very probable that quite a large number of open dimers are found present at this solution concentration, but without doubt the ring dimers still predominate. Further dilution with water leads to an increase in the number of dimers present as chainlets (II).

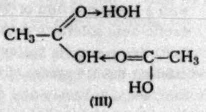


$$R{-}\underset{\displaystyle HO}{\underset{|}{C}}{=}O\cdots HO{-}\underset{\displaystyle O}{\underset{\|}{C}}{-}R$$

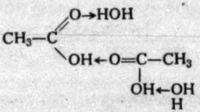
(II)

At a concentration of 83.5% the 1697 and 1665 cm^{-1} bands have nearly the same intensity; then the 1697 cm^{-1} band becomes more intense, while the 1665 cm^{-1} band becomes weaker (a shift of the band at 1660 to 1665, and of the band at 1770 to 1697 cm^{-1}, is explained by the mutual influence exerted by these bands on each other due to the small dispersion of the spectrograph).

At a concentration of 78.8% the line at 1667 cm^{-1} is still clearly seen;consequently, here a substantial number of ring dimers are contained in the solution. A new band appears at 1690 cm^{-1}. It is possible to assume that in this region of concentrations the water first adds according to schemes (III) and (IV), given by Murty and Seshadri [6].



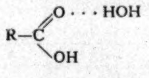
(III)



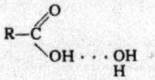
(IV)

At a concentration of 76.9% the band at 1700 cm^{-1} becomes narrower and the maximum at 1667 cm^{-1} disappears. Consequently, if any ring dimers did remain, then they are present in such small amount that it is difficult to detect them. Some authors [6, 17, 21-24] have shown the formation of the monohydrate at this concentration of acid.

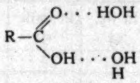
With further dilution, and specifically at an acid content of 73.9 and 71.3%, special changes in the configuration of the band at 1700 cm^{-1} fail to be observed. At this concentration there still remain some monohydrates as chain dimers, and as some authors believe, the chain dimers suffer cleavage with the formation of hydrates of the type of (V) and (VI) and subsequent formation of dihydrates of the type of (VII).



(V)



(VI)



(VII)

At a concentration of 65.1 and 62.8%,the band corresponding to the C=O group becomes sharper and narrower; according to the data of [21-24], dihydrates are formed in this region of concentrations.

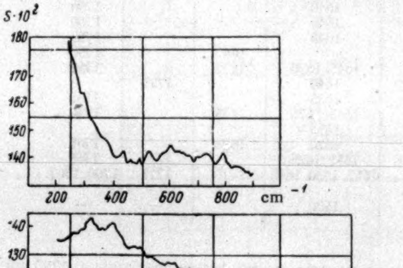


Fig. 2. Microphotometric spectral curve of a PRK-2 mercury lamp.

Beginning with a concentration of 60.3% a line appears at 1670 cm^{-1}. Apparently, this line belongs to the light source, since at low concentrations the lines of the light source steadily become more noticeable. It is possible that the bands at 1720 and 1750 cm^{-1} also belong to the light source. In any case, close maxima exist on the microphotometric spectral curve of the light source (Fig. 2). Unfortunately, we were unable to utilize the so-called "cold" mercury lamp.

With further dilution the maximum of the band, belonging to the C=O group, hardly changes and only its relative intensity gradually diminishes. It exists even down to 1.3%. At these concentrations a maximum is also seen at 1690 cm^{-1}.

In our opinion the band at 1690 cm^{-1} in acetic acid solution belongs to the C=O group to which the water had added through hydrogen bonding. Since this same maximum is also seen at an acetic acid concentration of 1.3%, it is possible to postulate that the bond with water in the carbonyl group continues to exist at least down to this concentration, where the amount of ions present is still very small.

From Fig. 1 it can be seen that the general maximum at 1700 cm^{-1}, beginning with a concentration of 78.8% and lower, in acetic acid solutions does not change its position. Most authors believe that it shifts with dilution toward greater frequencies. To be sure, there is hardly any data in the literature for concentrations below 20% and no systematic studies of solutions with close concentrations.

We will pass over to a description of the band at 1430 cm^{-1}. Different opinions exist as to which group is responsible for this band. Some authors [12, 16, 37] believe that it belongs to the CH$_2$ group. According to the data of [31], it disappears when a hydrogen in the CH$_3$ radical is replaced by deuterium. Edsall [32], however, believes that this frequency belongs to the carboxyl group. According to our data, it fails to shift clear down to a concentration of 1.3%, but beginning with 83.5%, additional maxima appear. It is possible to assume that this frequency at 1430 cm^{-1} belongs to either the C−O or the C−OH group (according to Karle and Brockway [33], the distance between atoms for C=O in the dimer is 1.25 A, and for C−O this distance is 1.36 A; consequently, the frequency for C−O should be smaller than for C=O).

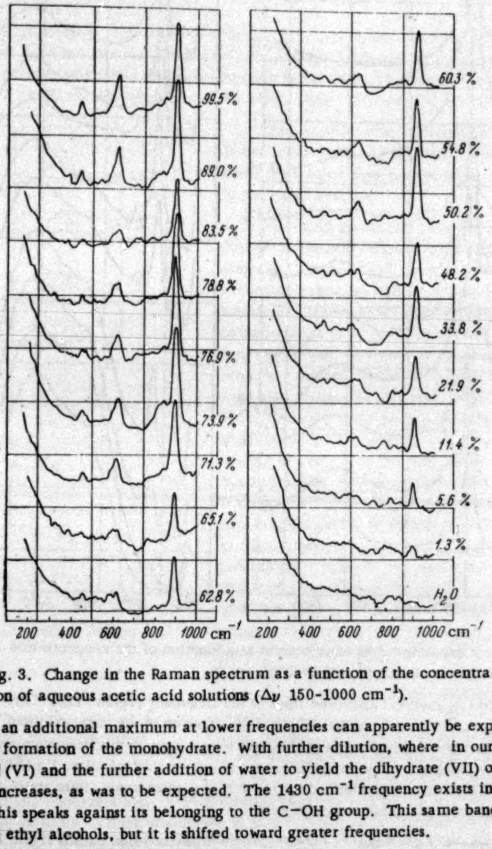


Fig. 3. Change in the Raman spectrum as a function of the concentration of aqueous acetic acid solutions ($\Delta\nu$ 150-1000 cm^{-1}).

The appearance of an additional maximum at lower frequencies can apparently be explained by a rupture of the ring dimer and the formation of the monohydrate. With further dilution, where in our opinion the formation of monomers (V) and (VI) and the further addition of water to yield the dihydrate (VII) occurs, the shift of the frequency gradually increases, as was to be expected. The 1430 cm^{-1} frequency exists in the spectrum of acetic anhydride [31]. This speaks against its belonging to the C−OH group. This same band is also present in the spectra of methyl and ethyl alcohols, but it is shifted toward greater frequencies.

Venkateswaran and Bhagavantam [28] considered the frequency at 1360 cm^{-1} as belonging to the C−OH group, since a band close to this is found in the alcohols. Other authors attributed it to the CH$_3$ group. The latter seems invalid to us, since, beginning with 48.2%, it disappears (which could not be if it belonged to the radical), and in place of it bands appear at 1345 and 1370 cm^{-1}, which possibly belong to the light source (Fig. 2). This can also be seen from Fig. 6, where the curves for dilute solutions are shown in greater detail (the photographs were taken on different plates). These bands, especially the band at 1370 cm^{-1}, are quite intense in the spectrum of water. It should be mentioned that the band at 1360 cm^{-1} is also present, with hardly any changes, in the spectrum of acetic anhydride [31]. Saksena [11] attributes the band at 1360 cm^{-1} to the symmetrical vibration of the carboxyl group.

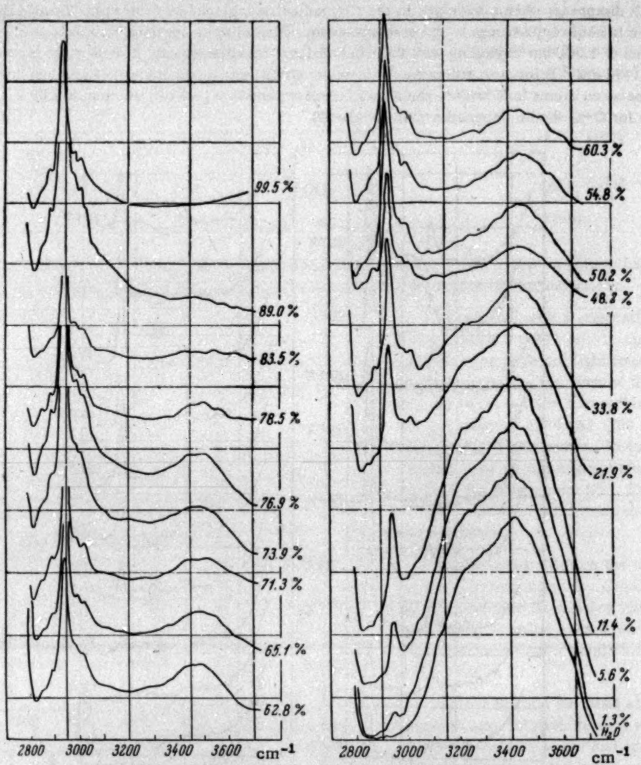


Fig. 4. Change inthe Ramanspectrum as a function of the concentration of acetic acid in water solution (Δν 2800-3750 cm^{-1}).

It is difficult to say anything about the lines in the frequency region 1250-1000 cm^{-1}. Some authors [28, 31] attributed the line at 1010 cm^{-1} to the deformation vibration of the carboxyl group. It is difficult to decipher these frequencies, since quite intense lines of the light source exist in this frequency region, and in character they resemble very closely the bands found in the spectrum of acetic acid (cf. Figs. 1 and 2). When the acid is diluted the intensity of these lines increases when compared with the other bands. Pure water also gives these bands. We believe that they are not attributable to acetic acid.

We will pass over to a discussion of Fig. 3. The most intense line on this figure is at 892 cm^{-1}. There are no special arguments relative to its origin. It is assumed to belong to the C−C bond [16, 28, 30]. This band completely fails to change in either position or contour on dilution and is still present at a concentration of 1.3%. To be sure, at this concentration it appears complex, but this complexity is only apparent, since the bands found in the spectrum of water or those of the light source are also present in the given region.

Of great interest is the behavior shown by the next most intense band at 617 cm^{-1}. It has a simple structure only in concentrated acetic acid (99.5%). Beginning with 89.0%, this band becomes broader due to an additional maximum on the side of the frequencies below 600 cm^{-1}, on dilution shifting to 590 cm^{-1}; this maximum remains when the acid concentration is decreased further. In the concentration region 65-60% acid a second maximum appears that is due to even smaller frequencies, and specifically at 580 cm^{-1}. On dilution the band at 590 cm^{-1} steadily becomes more noticeable, increasing in intensity when compared to the band at 617 cm^{-1}. At a concentration of 33.8% the bands at 617 and 590 cm^{-1} show almost the same intensity (cf. also Fig. 5), and at a concentration of 5.6% the intensity of the band at 590 cm^{-1} even predominates.

A special study of this band at 590 cm^{-1} was made by Leitman and Ukhodin [38], who studied the change in its intensity when the acid was diluted with water. According to their data, the intensity is greatly weakened at a concentration of 40%. This is in agreement with our data. Saksena [11], the same as Leitman and Ukhodin, believes that this band is attributable to association of the molecule (for trichloroacetic acid). According to the data of many authors, this band is absent in alcohols (cf., for example [39]) and in oxalic acid. It is also known [31] that this frequency changes when only the hydrogen atom in the carboxyl group of the acid is replaced by deuterium. Sverdlov [36] attributes this frequency to the deformation vibration of O−C−O.

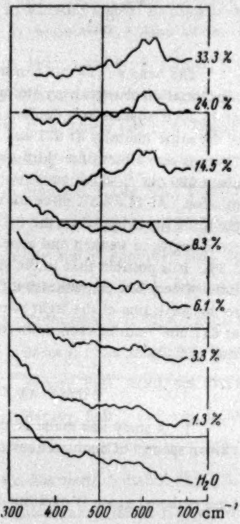


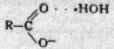
Fig. 5. Change in the Raman spectrum as a function of the concentration for aqueous acetic acid solutions ranging in concentration from 33.3 to 1.3%.

The behavior of this frequency is comparable to that of the C=O band, which changes with change in the hydrogen bonding in the acid on rupture of the ring dimer and in the formation of hydrates.

The band at 445 cm^{-1} also shows strong change with change in the acid concentration. Thus, at 99.5% it, the same as the band at 617 cm^{-1}, fails to have a complex structure. Beginning with a concentration of 89.0%, an additional maximum appears, but only its frequency is greater, being found at 460 cm^{-1}. This maximum is retained on further dilution. However, in the more dilute solutions a relatively intense maximum appears at 435 cm^{-1}. This band also changes its structure on dilution of the acid with water. An extremely intense band, shown in Fig. 4, appears at 2944 cm^{-1}; it belongs, as has been shown by a very large number of authors, to the CH_3 group. This band is complex: it also contains three weaker bands at 2880, 2990 and 3023 cm^{-1}. It is possible for the 5026 A mercury line (3046 cm^{-1} in the Raman spectrum) to be superimposed on the last band. All of these bands are quite fixed in their position. They can be seen clear down to an acetic acid concentration of 1.3%. The statement made by Batuev [15, 40] that the bands at 2990 and 3023 cm^{-1} belong to the frequency of the O−H group in the dimeric ring seems improbable, since it completely fails to change its position with change in the concentration, despite the rupture of the rings and further transformations of the acetic acid molecule into monomers with greater dilution. In addition, Batuev believes that a broad band is present at dilutions of the order of 10%, belonging to the O−H group of the polymer. However, a superimposition of the O−H band on the 2944 cm^{-1} band and its components is not seen at a single concentration. A well-defined minimum exists between the CH_3 and O−H bands, while in general there are no bands or lines whatsoever in concentrated acid. A well-defined minimum is present in the 3100-3600 cm^{-1} region. It could be mentioned that the higher the concentration of the solution, the greater is the shift of the O−H band toward greater frequencies. For example, in the spectrum of water the maximum is at approximately 3430 cm^{-1}, while in the spectrum of 78.8% acid it is at approximately 3550 cm^{-1}. This is a known fact.

We will now pass over to a discussion of the spectra of solutions with a low concentration, since such solutions are of especial interest to us. We repeated the photographing of acetic acid solutions on new plates and at smaller concentration intervals (Figs. 5 and 6).

The band, corresponding to the C=O group, can be seen even at the very low concentrations studied by us. It can be shown at 1.3%. At 33.0% it is sharply defined and has a general maximum at 1700 cm^{-1}. Besides this maximum, there are also maxima at 1710 and 1680 cm^{-1}. On further dilution the band retains its position to approximately a concentration of 8.3%; then the maximum at 1700 cm^{-1} vanishes, and only the maxima at 1690 and 1710 cm^{-1} remain, which are retained down to a concentration of 1.3%. The presence of a band at 1690 cm^{-1} can serve as evidence that water remains attached to the C=O group for quite a long time, despite the fact that dissociation begins with a concentration of 6.0%. If it is assumed that the band at 1430 cm^{-1} corresponds to the C–O bond, then water begins to be cleaved at approximately 24.0%, (the maximum at 1420 cm^{-1} vanishes) which is quite probable in connection with the further formation of ions of the hydrated form (VIII).



(VIII)

The band at 617 cm^{-1} in solutions of low concentration changes very strongly on dilution. At 33.3% it appears as a doublet (two maxima of of the same intensity at 617 and 590 cm^{-1}). There is also a hint of a third maximum at about 580 cm^{-1}, which becomes stronger with dilution. At 14.5% all three maxima have nearly the same intensity; then the maximum at 590 cm^{-1} begins to weaken and appears again at 1.3%. It is possible that in the spectra of solutions of very low concentration it is now due to the weak line of the light source. The band at 617 cm^{-1} can be seen down to a concentration of 3.3%.

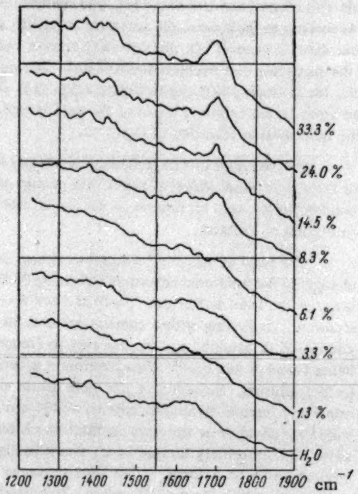


Fig. 6. Change in the Raman spectrum as a function of the concentration for aqueous acetic acid solutions ranging in concentration from 33.3 to 1.3%.

SUMMARY

1. A study was made of the change in the Raman spectra of aqueous acetic acid solutions as a function of the concentration (from 99.5% down to 1.3%).

2. The appearance of a maximum 1690 cm^{-1} in the band of the carbonyl group is explained by the formation of hydrates of acetic acid.

3. A change in the configuration of the band at 617 cm^{-1} on dilution of the acid with water proceeds simultaneously with a change in the hydrogen bonding in the acid. The band does not have structures in the ring dimer; on rupture of one hydrogen bond a maximum appears at about 600 cm^{-1}, which on further dilution shifts to 590 cm^{-1}, while in the concentration region of 65-60% (formation of dihydrates) still another maximum appears (at 580 cm^{-1}). As a result, the appearance of the band at 617 cm^{-1} is linked to the molecular structure of the acid.

4. The band at 1430 cm^{-1} (and possibly the band at 1360 cm^{-1}) we regard as belonging to either the C–O group or to the C–OH of the carboxyl. In the ring dimer this band does not have a complex structure. It does not change its position on dilution of the acid with water, but with dilution an additional maximum appears at lower frequencies, the position and relative intensity of which changes with change in the concentration.

5. Beginning with 78.8% and on further dilution a shift of the band at 1700 cm^{-1}, corresponding to the carbonyl group, fails to occur. This band can be seen down to a concentration of 1.3%.

6. The group of bands at 2944, 2880, 2990 and 3023 cm^{-1} remains completely fixed and does change its position at all dilutions, clear down to a concentration of 1.3%. Consequently, these bands without doubt belong to the acetic acid radical.

7. The band at 892 cm^{-1}, belonging to the C−C bond, also does not change on dilution down to a concentration of 1.3%.

8. The groups of bands near 1020 and 1105 cm^{-1}, which some authors ascribed to acetic acid, apparently belong to the light source.

Received January 29, 1957

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TERNARY RECIPROCAL SYSTEM OF SODIUM AND POTASSIUM FORMATES AND NITRATES

O. I. Dmitrevskaia

A study of the reaction of the sodium and potassium salts of fatty acids with nitrates in melts was directed toward obtaining data on the influence of complex-formation on the exchange process, on the direction of the exchange reaction, and also to determine the influence exerted by the chain length of the hydrocarbon radical of the fatty acid salt on the character of exchange and complex-formation.

EXPERIMENTAL

Method of Operation. The visual polythermal method of physicochemical analysis was used to make the study. The temperature when the first crystals appeared was measured using a nichrome-constantan thermocouple. The salts of c.p. quality were recrystallized and dried to constant weight; they had the following melting points: HCOONa 258°, HCOOK 167°, KNO_3 337°, $NaNO_3$ 308°.

Transitions in the solid state were observed for all of the salts: KNO_3 – at 124 and 316° [1-3], $NaNO_3$ – at 270° [2-4], and HCOONa – at 242° [5]; HCOOK has three transitions in the solid state at 60, 135 and 157° [5].

All of the compositions are expressed in mole percent.

TABLE 1

Binary Systems

HCOONa–$NaNO_3$		HCOOK–KNO_3				HCOONa–HCOOK			
% $NaNO_3$	temp.	% KNO_3	temp.	% KNO_3	temp.	% HCOOK	temp.	% HCOOK	temp.
0	258°	0	167°	50	172°	0	258°	65	179°
10	242	5	166	55	193	5	252	70	180
15	232	10	165	60	212	10	246	75	182
25	214	15	164	65	230	15	240	80	181
35	198	20	162	70	248	20	232	85	179
40	192	25	159	75	264	25	222	90	173
45	188	30	155	80	279	30	209	96	167
49	186	32.5	150	85	294	35	198	97	168
50	190	35	153	90	309	40	186	98	171
55	206	37.5	154	95	323	45	176	99	169
65	235	40	150.5	100	337	49.5	168	99.5	168
75	262	42	146	—	—	50	169	100	167
85	284	45	153	—	—	55	172	—	—
100	308	47.5	161	—	—	60	176	—	—

Binary Systems. 1. System HCOOK–KNO_3 was studied first. Here the compound 2HCOOK · KNO_3 is formed, which forms eutectics with the original components: at 150° and 67.5% HCOOK, and at 146° and 44% KNO_3 (Table 1, Fig. 1).

2. System HCOONa–$NaNO_3$ had been studied earlier [6]; it forms a eutectic at 186° and 49% $NaNO_3$ (Table 1, Fig. 1).

3. System HCOOK–HCOONa was studied by us for the first time; the compound 3HCOOK · HCOONa is formed here, which with the original components gives eutectics at 168° and 49.5% HCOOK, and at 167° and 4% HCOONa (Table 1, Fig. 1).

4. System $NaNO_3$–KNO_3 has been studied by many authors [2, 7-10], and we utilized the data given in [2]. A continuous series of solid solutions is formed in this system with a melting point minimum at 223° and 50% KNO_3 (Fig. 1.).

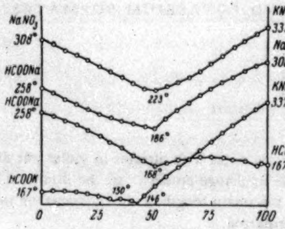


Fig. 1. Fusion diagram of binary systems.

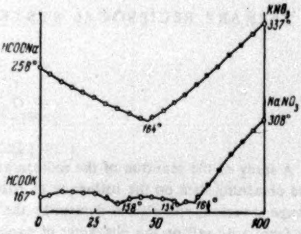


Fig. 2. Fusion diagram of diagonal sections.

Diagonal Sections. 1. HCOONa–KNO_3 is a stable diagonal with eutectic point at 164° and 48% KNO_3. The polymorphous transformation of HCOONa, discovered by N. M. Sokolov [5], is observed on the HCOONa branch at 242°. The KNO_3 branch is curved somewhat under the influence of solid solutions Na, K ‖ NO_3 (Table 2, Fig. 2).

2. HCOOK–$NaNO_3$ is an unstable diagonal. The fusion curve has four branches of crystallization, intersecting in three points: at 158° and 34.5% $NaNO_3$, at 155° and 63% $NaNO_3$, and at 164° and 69% $NaNO_3$ (Table 2, Fig. 2).

TABLE 2

Diagonal Sections

Stable						Unstable					
HCOONa–KNO_3						HCOOK–$NaNO_3$					
% KNO_3	temp.	% KNO_3	temp.	% KNO_3	temp.	% $NaNO_3$	temp.	% $NaNO_3$	temp.	% $NaNO_3$	temp.
0	258°	35	188°	75	235°	0	167°	34.5	158°	65	158°
2.5	252	40	180	80	252	2.5	169	35	159	67.5	163
5	242	45	172	85	269	5	170	37.5	162	69	164
7.5	241	48.5	164	90	288	10	174	40	164	70	168
10	236	50	166	95	307	15	176	45	166	75	195
15	226	55	180	96.5	316	20	176	50	166	80	224
20	218	60	193	97.5	322	25	173	55	164	90	272
25	208	65	205	100	337	30	167	60	160	95	292
30	199	70	220	—	—	32.5	163	63	154	100	308

Fusion Diagram of Reciprocal System. Based on the results of studying the binary systems, and the diagonal and 23 internal sections (Figs. 3-6), we constructed a projection of the joint crystallization curves on the plane of the polytherm of the binary system $NaNO_3$–KNO_3 (Fig. 8); this made it possible to determine the positions of the ternary and isothermal points on the joint crystallization curves. A projection of the liquidus diagram of the ternary reciprocal system on the composition square, with the isotherms drawn at 20° intervals, is shown in Fig. 7. The system is irreversible-reciprocal with a stable diagonal, which agrees with the conditional heat effect for the exchange reaction, equal to 3.37 kcal/equiv on the side of the stable pair HCOONa and KNO_3:

$$\underset{160.7}{HCOOK} + \underset{111.72}{NaNO_3} \longrightarrow \underset{157.7}{HCOONa} + \underset{118.09}{KNO_3}$$

The heats of formation were taken from a handbook [11]. Although the conditional thermochemical effect for the exchange reaction is small, and complex-formation occurs at the sides and inside the system, still the system belongs to the class of diagonal systems, and complex-formation does not change the direction of the exchange reaction.

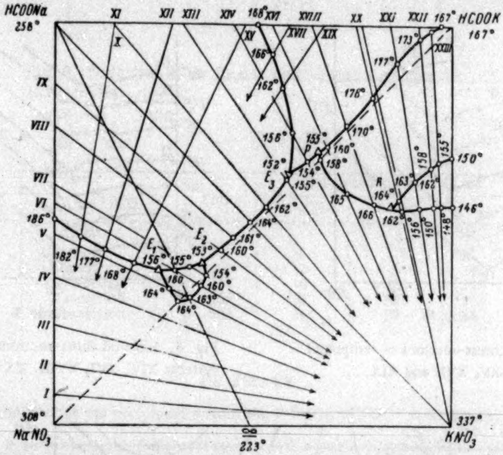

HCOONa
258°
XI
XII
XIII
XIV
168°
XVI
XVIII
XX
XXI
XXII
167°
HCOOK
167°
X
XV
XVII
XIX
XXIII
IX
VIII
VII
VI
186°
V
IV
III
II
I
308°
NaNO₃
223°
337°
KNO₃
150°
146°
E₁
E₂
E₃
P
R
182°
177°
168°
156°
155°
153°
160°
161°
164°
162°
154°
163°
152°
158°
170°
176°
177°
173°
166°
165°

Fig. 3. Arrangment of internal sections in the reciprocal system Na, K‖NO_3, HCOO.

The compound 2HCOOK · KNO_3, formed on the HCOOK−KNO_3 side, tapers out in the reciprocal system and ceases to exist in the transition point R at 164°. The eutectics of the binary system HCOOK−KNO_3 have melting points that are below either the transition point or the melting point of the ternary eutectic. Point R in the reciprocal system is a point of double rise.

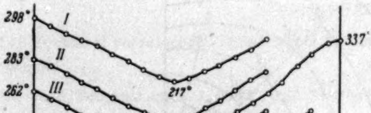


Fig. 4. Internal cross-sections of reciprocal systems I-IX.

The liquidus surface of the reciprocal system is divided into six crystallization fields: 1) field HCOONa, 2) field of the compound 3HCOOK · HCOONa, 3) field HCOOK, 4) field of the compound 2HCOOK · KNO_3, 5) field of solid solutions Na, K ‖ NO_3, and 6) a field, apparently belonging to the compound $NaNO_3$ · KNO_3, which is formed, according to the data of A. G. Bergman, in the decomposition of solid solutions Na, K ‖ NO_3 when the temperature is lowered to 180°, while in the side system it appears very vaguely at 165-175° in the region of the solid state [14]. In the investigated system it appeared at 165°. Similar fields were also observed in the systems: Na, K ‖ NO_3, CH_3COO [12], Na, K ‖ NO_3, SO_4 [13] and Na, K ‖ NO_3, NO_2 [14], but under the stabilizing influence of the acetates and nitrates they appeared on the liquidus surface at a higher temperature; it is obvious that the formates failed to show a stabilizing influence in the investigated system.

The compound 3HCOOK · HCOONa, congruent on the binary side HCOOK−HCOONa, becomes incongruent in the reciprocal system. Triangulation of the system is accomplished by the stable diagonal HCOONa−KNO_3 (stable cross section) and two unstable cross sections: one starts from the zone of the compound $NaNO_3 \cdot KNO_3$ and goes to the HCOONa vertex, while the other starts from the zone of the compound 3HCOOK · HCOONa and goes to the KNO_3 vertex.

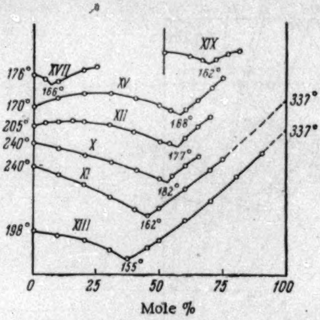


Fig. 5. Internal cross-sections of reciprocal systems X-XIII, XV, XVII and XIX.

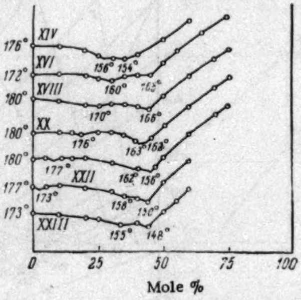
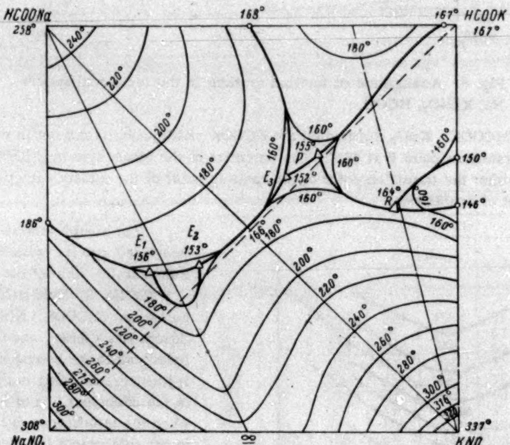


Fig. 6. Internal cross-sections of reciprocal systems XIV, XVI, XVIII, XX−XXIII.



HCOONa
258°
168°
167° HCOOK
167°
240°
220°
200°
180°
180°
160°
155°
P
E3
152°
160°
160°
160°
150°
150°
164°
R
160
146°
160°
186°
E1
156°
E2
153°
166°
180°
200°
220°
240°
260°
280°
300°
316°
320
180°
200°
220°
240°
260°
275°
280°
300°
308°
NaNO3
∞
223°
337°
KNO3

Fig. 7. Projection of the surface of crystallization of the reciprocal system Na, K ‖ NO_3, HCOO on the composition square.

The composition square of the reciprocal system is divided into four phase triangles: 1) $NaNO_3$−$NaNO_3 \cdot KNO_3$−HCOONa, 2) $NaNO_3 \cdot KNO_3$−HCOONa−KNO_3, 3) KNO_3−HCOONa−3HCOOK · HCOONa, 4) 3HCOOK · HCOONa−HCOOK−KNO_3.

A ternary invariant point corresponds to each triangle: E_1, E_2, E_3 and P, the temperatures and compositions of which are shown in Table 3.

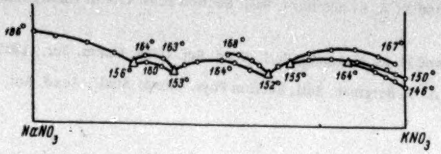


Fig. 8. Projection of the lines of joint crystallization on the $NaNO_3-KNO_3$ side.

TABLE 3

Point	Type	Temp.	Composition (in mole %)			
			HCOONa	HCOOK	KNO_3	$NaNO_3$
E_1	Eutectic	156°	38.5	—	27	34.5
E_2	Eutectic	153	42	—	36.5	21.5
E_3	Eutectic	152	40	23.5	36.5	—
P	Transition	155	35	31.5	33.5	—
R	Transition	164	16	39	45	—

SUMMARY

1. The fusion diagram of the reciprocal system Na, K ‖ NO_3, HCOO was studied.

2. The system is an irreversible-reciprocal system with a stable diagonal. Solid solutions Na, K ‖ NO_3 are stable inside the system down to 165°, while below this temperature they decompose with the formation of compound $NaNO_3 \cdot KNO_3$.

3. A point of double rise is present in the system.

4. Complex-formation in the system does not change the direction of the exchange reaction.

Received February 18, 1957

Smolensk State Medical Institute

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REDUCTION OF NITROPHENOLS AT A MULTIDROP MERCURY CATHODE

L. N. Vertiulina and N. I. Maliugina

A study of reduction at a dropping-mercury electrode was made by various authors for the purpose of quantitatively determining and establishing the mechanism of the reduction.

Kolthoff and Lingane [1] state that the reduction of aromatic nitro compounds does not go by the scheme proposed by Haber [2], but instead that it proceeds with the addition of 4 electrons to phenylhydroxylamine, in which connection phenylhydroxylamine in acid medium is reduced to aniline, and a second wave is observed on the polarogram. I. A. Korshunov and A. S. Kirillova [3] also came to the same conclusions.

In the early studies on the polarographic reduction of nitrophenols [4] only the reduction potentials of the indicated compounds are given, determined by the method of tangents.

Later Astle and McConnell [5] reduced o-nitrophenol, but the results obtained by them were not confirmed by Stocesova [6], who believes that in neutral medium (pH 6) o-nitrophenol, in contrast to p-nitrophenol, is reduced with the addition of 4 electrons. In either more acid or more alkaline medium the o-nitrophenol is reduced with the addition of 6 electrons. The author explains this by an acid-base catalyzed transformation of o-hydroxyphenylhydroxylamine to the quinone imine, which is then reduced further.

Pearson [7], who studied the reduction of o-, m- and p-nitrophenols in the presence of 8% ethyl alcohol in buffer solutions with pH ranging from 2 to 12, states that in solutions with pH 2 the nitrophenols are reduced with the addition of 6 electrons, while in alkaline medium both o- and p-nitrophenol are also reduced with the addition of 6 electrons, whereas m-nitrophenol is reduced with the addition of only 4 electrons.

Similar results were also obtained by other authors in the presence of 10% ethyl alcohol [8] and in the absence of alcohol [9].

A determination of the composition of the reduction products represents great theoretical and practical interest in the problems dealing with an elucidation of the reduction mechanism of organic compounds. The use of a multidrop mercury cathode for this purpose is convenient, since it permits accumulating the reduction products in amounts sufficient for analysis. In addition, as had been shown by Vodzinskii and Korshunov [10], the electroreduction conditions using a multidrop cathode are quite close to the electroreduction conditions that prevail when the ordinary dropping-mercury cathode is used.

Using the multidrop mercury cathode, we subjected the o-, m- and p-nitrophenols to reduction in acidified aqueous and aqueous-alcohol solutions of sodium sulfate, having a pH ranging from 2 to 2.5, in order to establish the mechanism of their polarographic reduction. Another reason for using aqueous and aqueous-alcohol solutions was to determine the effect exerted by alcohol as a solvent on the reduction of nitrophenols, an effect that has been mentioned by a number of authors [11, 12].

EXPERIMENTAL

We used the apparatus with a multidrop mercury cathode described in [13], which was modified by us slightly in order to make it suitable for our investigations.

In order to compare the results obtained in the electroreduction of nitrophenols in aqueous and in aqueous-alcohol solutions we maintained the electrolysis conditions constant. The electrolysis was run in acidified aqueous and aqueous-alcohol (25% ethyl alcohol by volume) solutions with pH ranging from 2 to 2.5 at 18-20°. The course of the electrolysis was followed by the value of the limiting current on the polarograms, for which samples were taken at 1-2 hour intervals. At the end of reduction the products were analyzed and the yield of compounds was calculated on the basis of the amount of nitro compound taken for reduction.

The electrolysis was run at a potential slightly higher than the potential of the limiting current, and specifically, for p-nitrophenol at 2.2 v, and for m- and o-nitrophenols at 1.8 v.

During electrolysis the p-nitrophenol solution became dark brown, and a dark brown precipitate deposited. It was found that the electrolyte contains p-aminophenol and p-quinone imine, while the precipitate proved to be p-aminophenol. That p-aminophenol was present in both the electrolyte and precipitate was established by preparing the benzoyl derivative [14]. The melting points of the benzoyl derivatives, and also the mixed melting points of the benzoyl derivatives of the investigated specimens and of pure p-aminophenol, showed quite satisfactory agreement with the literature data, according to which the melting point of the benzoyl derivative of p-aminophenol is 234° [14]. The benzoyl derivatives obtained by us from the precipitate and from the solution, and also their mixtures with the authentic material, had m.p. 230 ± 1°. To quantitatively determine the amount of p-aminophenol in the precipitate and in the electrolyte we used the GOST method [15], based on the reaction of aromatic amines with nitrous acid. p-Quinone imine, formed in small amounts in the electrolysis of p-nitrophenol, did not interfere with the determination of p-aminophenol. The presence of the unstable intermediate product – p-quinone imine – was determined both qualitatively and quantitatively by the amount of iodine liberated, using the method proposed by Bauer [16].

Analysis Results for the Reduction Products of Nitrophenols

Compound	Aqueous solution with pH 2.0			Aqueous-alcohol solution with pH 2.5		
	amount (in %)					
	aminophenol	quinone imine	hydroxylamino derivative	aminophenol	quinone imine	hydroxylamino derivative
p-Nitrophenol	82	11	–	48	5	–
o-Nitrophenol	88	4	–	89	5	–
m-Nitrophenol	46	–	48	37	–	37

Analysis of the products of the electroreduction of o-nitrophenol at a multidrop mercury cathode revealed that o-aminophenol and a quinoid derivative of o-nitrophenol are present in the electrolyte. From the electrolyte we isolated the benzoyl derivative of o-aminophenol with m.p. 179 ± 1°, close to the data given in the literature [14] (184°, 182°).

The same as in the case of p-aminophenol, the amount of o-aminophenol was quantitatively determined by the diazotization method. The presence of o-quinone imine was indicated by the red color of the solution, inherent, as is known, to o-quinone derivatives. A quantitative determination of the amount of o-quinone imine was made in the same way as for p-quinone imine.

Qualitative analysis of the reduction products of m-nitrophenol revealed the presence of m-aminophenol and of the hydroxylamino derivative of m-nitrophenol.

The benzoyl derivative of m-aminophenol had m.p. 150°, which is in fairly good agreement with the literature data [14].

We were unable to obtain the benzoyl derivative of the hydroxylamino derivative of m-nitrophenol due to its instability in the presence of atmospheric oxygen.

A quantitative analysis of the reduction products of m-nitrophenol was made by the method described in [17], which method was modified by us slightly in that hydrogen was blown through the silver nitrate solution for 1 hour to remove dissolved oxygen before the silver nitrate solution was mixed with the analyzed solution. It was shown that under the analysis conditions m-aminophenol fails to deposit silver when kept in the dark for a day.

In contrast to the o- and p-nitrophenols, a quinoid compound is not formed in the reduction of m-nitrophenol, since m-quinones do not exist, as is indicated in the literature [18].

The analysis results for the reduction products of the p-, o- and m-nitrophenols in aqueous and aqueous-alcohol solutions at a multidrop mercury cathode are given in the table.

The percent yield of reduction products is the average of several experiments. The determination accuracy of the reduction products was 5-6% (relative).

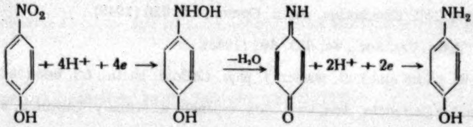
As can be seen from the data in the table, for the p- and m-nitrophenols the yield of reduction products at a multidrop mercury cathode in aqueous-alcohol solutions with pH 2.5 is less than in aqueous solutions.

In the case of o-nitrophenol the yields of reduction products in aqueous-alcohol and aqueous solutions are the same.

DISCUSSION OF RESULTS

The obtained data permit the conclusion that p-nitrophenol is mainly reduced to p-aminophenol, and here p-quinone imine is formed as intermediate product; o-nitrophenol is reduced to o-aminophenol, and in this case the intermediate reduction product is o-quinone imine. The reduction products of m-nitrophenol were the hydroxylamino derivative and m-aminophenol.

The scheme for the reduction of nitrophenols in both aqueous and aqueous-alcohol solutions can be depicted on the example of p-nitrophenol.



The transformations for the ortho and meta isomers can be depicted in similar manner (for the meta isomer without the quinone imine).

In the reduction of the o- and p-nitrophenols the intermediate compounds – the o- and p-quinone imines – are formed in small amounts. Their accumulation in substantial amount does not occur for the reason that they are readily reduced at a multidrop mercury cathode, which is in agreement with the data of the polarographic studies made on compounds having the quinoid bond [1].

m-Aminophenol and the hydroxylamino derivative of m-nitrophenol are formed in nearly equal amounts when m-nitrophenol is reduced at a multidrop mercury cathode under the conditions investigated by us.

The substantial formation of the hydroxylamino derivative of m-nitrophenol can be explained by the fact that its further reduction is evidently made difficult.

It is possible that in this case the potential of the cathode exerts an influence on the reduction rate of the hydroxylamino derivative of m-nitrophenol. A similar influence of the cathode potential on the reduction process was observed by L. I. Antropov and N. T. Vagramian when they studied the reduction of phenylhydroxylamine at a platinum cathode in alcohol-sulfuric acid solutions [19].

The decrease in the yield of products when the p- and m-nitrophenols were reduced in aqueous-alcohol solutions, observed in our investigations, is probably explained by the formation of an intermolecular hydrogen bond, which in aqueous-alcohol solutions is formed with involvement of the alcohol molecule, and this bond, being more stable than the one obtained in aqueous solutions, makes the reduction of the indicated compounds difficult [20].

o-Nitrophenol forms an intramolecular hydrogen bond, which, as is known [1, 20], facilitates reduction of the nitro group in both aqueous and aqueous-alcohol solutions. As a result, a decrease in the yield of reduction products in aqueous-alcohol solutions is not observed in this case.

The authors wish to thank I. A. Korshunov for his valuable advice in the execution of the present work.

SUMMARY

1. As the result of studying the reduction of the o-, m- and p-nitrophenols at a multidrop mercury cathode it was found that nitrophenols in aqueous and aqueous-alcohol solutions with pH from 2 to 2.5 are reduced mainly to o- and p-aminophenols. p- and o-quinone imines, obtained in small amounts, are formed as intermediate products. In the case of m-nitrophenol the reduction products are the hydroxylamino derivative of m-nitrophenol and m-aminophenol, formed in nearly equal amounts.

2. For the p- and m-nitrophenols the yields of reduction products at a multidrop mercury cathode are less in aqueous-alcohol solutions than in aqueous solutions; for o-nitrophenol the yield is the same in both media.

Received February 26, 1957 Gorki State University

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POLAROGRAPHIC STUDY OF AMINOACETOPHENONES

V. D. Besuglyi, V. N. Dmitrieva and V. V. Dorofeev

Giacometti and Del Marco [1] studied the polarographic behavior of p-acetophenylhydroxylamine and p-aminoacetophenone in buffer solutions with various pH values. The other aminoacetophenone isomers have not been subjected to polarographic study by anybody, although a detailed study of them would permit elucidating the influence exerted by the position of the NH_2 group on the reduction of the carbonyl group in aminoacetophenones.

The reduction of acetophenone and some of its derivatives has been studied in a number of papers [2-8]; here it was established that the reduction of acetophenone proceeds by different mechanisms in acid and in alkaline medium, and that two waves are observed in a certain pH range.

The polarographic behavior of o-, p- and m-aminoacetophenone was studied in the present paper.

EXPERIMENTAL

o-Aminoacetophenone was synthesized by the following scheme [12]

$$C_6H_5CH{=}CHCOOH \xrightarrow{HNO_3} NO_2C_6H_4CH{=}COOH \xrightarrow{Br_2} NO_2C_6H_4(CHBr)_2COOH \xrightarrow{NaOH}$$

$$\longrightarrow NO_2C_6H_4C{\equiv}CCOOH \xrightarrow{t^\circ} NO_2C_6H_4C{\equiv}CH \xrightarrow{H_2} NH_2C_6H_4C{\equiv}CH \longrightarrow NH_2C_6H_4COCH_3$$

The para isomer is formed together with o-aminoacetophenone under the indicated conditions.

The o- and p- isomers were separated during the synthesis: after reducing the nitrophenylacetylene the para isomer crystallized from the mixture of o- and p-aminophenylacetylenes, and this on hydration with dilute sulfuric acid, followed by isolation of the amine, gave p-aminoacetophenone with m.p. 106°. The yield of o-aminoacetophenone was about 8% when calculated on the cinnamic acid. o-Aminoacetophenone was also obtained from o-nitrobenzoic acid through o-nitrobenzoylacetoacetic ester [9].

m-Aminoacetophenone was obtained by the reduction of m-nitroacetophenone with ammonium sulfide, using the Ruppe, Braun and von Zembruski method [10], and was purified by repeated recrystallization from either water or dilute alcohol. The product was obtained as scaly plates with a slight yellow tinge and m.p. 99.2°.

p-Aminoacetophenone was obtained by the acetylation of acetanilide with acetyl chloride [11] in acetic anhydride, followed by hydrolysis of the N-acetyl derivative of p-aminoacetophenone, and then isolation of the p-aminoacetophenone, which was obtained as colorless prisms with m.p. 106°.

The polarographic measurements were made using a FG-8 polarograph with dropping-mercury electrode, the latter having the following characteristics: $m = 1.222$ mg/sec., $t = 2.0$ sec., $m^{2/3}t^{1/6} = 1.29\ mg^{2/3}\ sec.^{1/6}$ ($E = -1.9$ v).

The experiments were run at 18-20°. As a background for the polarography we used: 1) 0.1 N solution of KCl, Li_2SO_4 and $(CH_3)_4NI$; 2) buffer solutions: in the acid region, HCl + KCl; in the region of medium pH values, acetic acid + sodium acetate; in the region of medium and high pH values we also used universal buffer mixtures composed of phenol + phosphoric acid + acetic acid + NaOH. All of the solutions contained from 2 to 8% of C_2H_5OH in water.

In measuring the half-wave potentials a saturated calomel electrode was used as the reference.

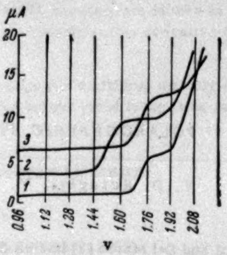

Fig. 1. Polarographic waves of aminoacetophenones (concentration 1.34 mmoles/liter) with a background of 0.1 N Li_2SO_4.
1) o-aminoacetophenone,
2) m-aminoacetophenone,
3) p-aminoacetophenone.

As the results of polarographing with a background of 0.1 N KCl, 0.1 N Li_2SO_4, 0.1 N $(CH_3)_4NI$, etc., showed, all three isomeric aminoacetophenones are reduced at the dropping-mercury electrode. Here for m-aminoacetophenone in the indicated solutions $E_{1/2} = -1.53$ v, while for the o- and p- isomers the half-wave potentials coincide and are equal to −1.71 v (Fig. 1).

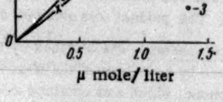

Fig. 2. Linear calibrations of aminoacetophenones with a background of 0.1 N Li_2SO_4.
1) o-aminoacetophenone,
2) m-aminoacetophenone,
3) p-aminoacetophenone.

TABLE 1

Values of the Half-Wave Potentials of o-, m- and p-Aminoacetophenones in Buffer Solutions With Various pH Values

Isomer	pH												
	1.6	2.2	3.72	4.85	5.11	5.74	6.45	6.92	7.54	8.3	9.4	10.7	11.36
o-Aminoacetophenone	−1.04	−1.07	−1.15	−1.24	−1.31	−1.41	−1.46	−1.49, −1.70	−1.55, −1.70	−1.71		−1.71	
m-Aminoacetophenone	−0.96	−1.00	−1.11			−1.21	−1.38	−1.39, −1.53	−1.41, −1.53	−1.53	−1.53		−1.53
p-Aminoacetophenone	−0.99	−1.08	−1.16			−1.38	−1.48	−1.50, −1.71	−1.56, −1.71	−1.71	−1.71		−1.71

The values of the half-wave potentials for all three isomers with a background of buffer solutions with various pH values are shown in Table 1.

The changes in the height of the waves as a function of the pH are shown in Table 2. The linear calibrations of the aminoacetophenones with a background of 0.1 N Li_2SO_4 are shown in Fig. 2.

TABLE 2

Height of the Waves of o-, m- and p-Aminoacetophenone at Various pH Values

Isomer	pH	C (m-mole/ / liter)	Height of wave (mm)		C (m-mole/ / liter)	Height of wave (mm)	
			1st wave	2nd wave		1st wave	2nd wave
o-Amino-aceto-phenone	1.6	0.99	15		1.34	20.5	
	2.2	0.99	14.5		1.34	19	
	3.72	0.99	13		1.34	18	
	8.3	0.99		11.5	1.34		15.5
	10.7	0.99		11.5	1.34		15.5
m-Amino-aceto-phenone	1.6	0.67	11		1.34	22	
	2.2	0.67	11		1.34	22	
	3.72	0.67	11		1.34	22	
	5.57	0.67	10.5		1.34	21	
	9.4	0.67		10.5	1.34		21
	11.36	0.67		10.5	1.34		21
p-Amino-aceto-phenone	1.6	0.67	11.5		1.34	22.5	
	2.2	0.67	11.5		1.34	22.5	
	3.72	0.67	11		1.34	22	
	5.57	0.67	11		1.34	21.5	
	9.4	0.67		11	1.34		21.5
	11.36	0.67		11	1.34		21.5

o-Aminoacetophenone. One well defined polarographic wave is observed in acid medium with a background of buffer solutions with pH ranging from 1.6 to 6.45, and the half-wave potential increases with rise in pH from −1.04 to −1.46 v (Fig. 2). When the polarographing was with a background of 0.1 N solutions of $(CH_3)_4NI$, Li_2SO_4 and KCl, and also with a background of alkaline buffer solutions with pH > 8, again only one polarographic wave was observed with $E_{1/2} = -1.71$ v, and the reduction potential did not change with further increase in the pH. This

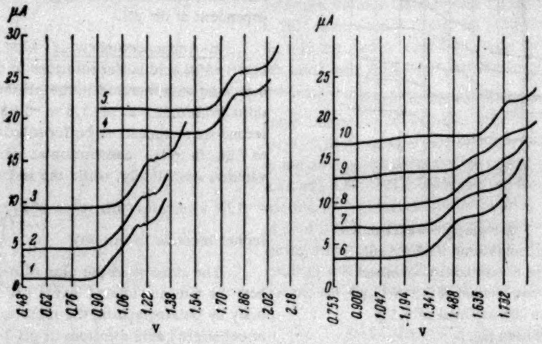

Fig. 3. Polarographic waves of o-aminoacetophenone with a background of buffer mixtures with various pH values. Concentration 1.34 mmoles/ liter: 1) pH 1.6, 2) pH 2.2, 3) pH 3.72, 4) pH 8.3, 5) pH 10.7; concentration 1.18 mmoles/ liter: 6) pH 5.74, 7) pH 6.45, 8) pH 6.92, 9) pH 7.54, 10) pH 8.00.

corresponds to two different polarographic waves. They are observed for o-aminoacetophenone simultaneously in buffer solutions with $6.9 < \mathrm{pH} < 8$; in this connection the potential of the first wave shows a shift when the pH is increased, while the potential of the second wave remains practically constant. Both of these waves are observed simultaneously when o-aminoacetophenone is polarographed with a background of unbuffered acid solutions. By adding a small amount of 0.1 N HCl solution to 0.1 N Li_2SO_4 solution, containing about 1.25 mmoles/liter of o-aminoacetophenone, it becomes possible to follow the rise of the first wave and the disappearance of the second wave (Fig. 4). Thus, for example, when 0.2 ml of 0.1 N HCl solution is added to 10 ml of 0.1 N Li_2SO_4 solution, containing o-aminoacetophenone, besides the second wave (with $E_{1/2} = -1.71$ v), there appears a wave with $E_{1/2} = -1.17$ v. The latter is the first wave that is observed on the polarograms obtained in buffered acid solutions. When 0.3 ml of 0.1 N HCl solution is added the height of this wave increases, while the second wave disappears completely. With further additions of acid the height of the first wave remains unchanged, and still another wave appears, corresponding to hydrogen discharge (the height of this wave is proportional to the concentration of the acid).

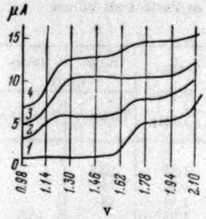

Fig. 4. Polarographic waves of a solution containing 1.25 mmoles/liter of o-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A (pH 6.22), 2) 10 ml A + 0.2 ml B (pH 3.28), 3) 10 ml A + 0.4 ml B (pH 3.25), 4) 10 ml A + 0.5 ml B.

The maximum height of the first wave is slightly greater than the sum of the heights of both waves, which in turn is slightly greater than the height of the second wave, obtained in the absence of HCl, as can be seen from the polarograms shown in Fig. 4.

A slight reduction in its height with increase in pH is observed for the first curve with a background of buffered solutions (Table 2). The height of the second wave is independent of the pH.

m-Aminoacetophenone. One polarographic wave is observed in acid buffer solutions in the pH range of 1.6 to 6.45, and with increase in the pH the half-wave potential shifts from 0.96 v at pH 1.6 to −1.38 v at pH 6.15. A second wave appears in buffer solutions with pH from 6.92 to 7.54, in which connection at pH > 8 the first wave vanishes completely, while the second wave with $E_{1/2} = -1.53$ v remains (this value of $E_{1/2}$ does not change with further increase in the pH).

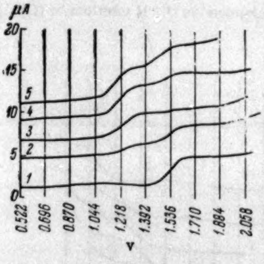

Fig. 5. Polarographic waves of a solution containing 0.67 mmole/liter of m-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A, 2) 10 ml A + 0.2 ml B, 3) 10 ml A + 0.4 ml B, 4) 10 ml A + 0.5 ml B, 5) 10 ml A + 0.6 ml B.

The same as in the case of o-aminoacetophenone, both the first and second waves can be obtained simultaneously by polarographing the meta isomer with a background of unbuffered acid solutions at pH 3-5.5. From Fig. 5 it can be seen that the gradual addition of 0.1 N HCl solution to m-aminoacetophenone with a background of Li_2SO_4 solution leads to the appearance of the first wave, the height of which increases as the pH of the solution decreases. In this connection the height of the second wave decreases in such manner that the sum of the height of the two waves remains constant. The height of the first wave no longer changes after the second wave has disappeared. Further increase in the acidity leads to the appearance of the hydrogen wave.

When m-aminoacetophenone is polarographed with a background of various buffer solutions it can be seen that the height of both the first and second waves is independent of the pH.

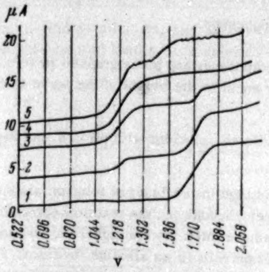

Fig. 6. Polarographic waves of a solution containing 1.34 mmoles/ /liter of p-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A, 2) 10 ml A + 0.1 ml B, 3) 10 ml A + 0.3 ml B, 4) 10 ml A + 0.5 ml B, 5) 10 ml A + 0.7 ml B.

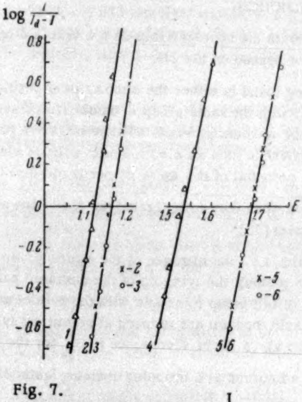

Fig. 7.
Relationship between $\log \frac{I}{I_d - I}$ and E.
1) m-aminoacetophenone, pH 3.37,
2) o-aminoacetophenone, pH 3.37,
3) p-aminoacetophenone, pH 3.37,
4) m-aminoacetophenone, pH 8.3,
5) o-aminoacetophenone, pH 8.3,
6) p-aminoacetophenone, pH 8.3.

p-Aminoacetophenone. The behavior of p-aminoacetophenone at the dropping-mercury electrode almost completely duplicates the behavior of the ortho isomer (Table 1). One wave (the first) is observed with a background of buffer solutions with pH 1.6-6.45. The value of $E_{1/2}$ changes with rise in the pH from −0.99 v at pH 1.6 to −1.48 v at pH 6.45, while a second wave with $E_{1/2} = -1.71$ v appears in alkaline buffer solutions (pH> 8). Both waves are observed simultaneously for the para isomer in buffer solutions with pH 6.92-7.54; in this connection the height of the second wave at pH 7.54 is lower than in the case of the other two isomers. The first and second waves appear simultaneously with a background of unbuffered acid solutions (Fig. 6). The sum of the heights of both p-aminoacetophenone waves remains constant, and is equal to the height of each of them singly in the absence of the other wave.

The relationships between E and $\log \frac{I}{I_d - I}$ for the investigated isomers are shown in Fig. 7. The slope of the straight lines on this graph shows that in all cases $\alpha < 1$, i.e., the reduction of the aminoacetophenones in both acid and alkaline media is an irreversible process.

Using the Ilkovic equation, we determined the number of electrons involved in the reduction of the aminoacetophenones at the dropping-mercury electrode. For the calculations we took the diffusion coefficient equal to 0.834×10^{-5} sq cm/sec.* Then the following values are obtained for n in the Ilkovic equation: 2.24 for the para, 2.30 for the meta, and 2.18 for o-aminoacetophenone.

The constants of the diffusion current for the investigated isomers in the alkaline region are equal to 3.74 for meta, 3.84 for para, and 2.89 for o-aminoacetophenone. In the acid region they are respectively equal to 3.92, 4.01 and 3.82. For o-aminoacetophenone the slight reduction in the value of the constant of the diffusion current in acid medium is apparently associated with the fact that during storage this isomer showed some tarring, and as a result of this its actual concentration was reduced. This tarring was not observed in the case of the other isomers.

DISCUSSION OF RESULTS

Generalizing the obtained results, it is possible to make the following conclusions. The same as is true with other acetophenone derivatives, the reduction of the aminoacetophenones proceeds by different mechanisms in acid and in alkaline media, in which connection the half-wave potentials have different values in acid and in alkaline media. The indicated circumstance leads to the situation that only one wave is observed in buffer solutions with pH < 6.5. With change in the pH of the buffer solution the $E_{1/2}$ shifts by 0.06-0.08 toward negative potentials per pH unit. In buffer solutions with pH > 8 one wave with $E_{1/2} = -1.71$ v is observed in the case of the o- and p-aminoacetophenones, and with $E_{1/2} = -1.53$ v in the case of m-aminoacetophenone.

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* Obtained by computation from the value of the diffusion coefficient of the benzoate ion in the same medium, equal to 0.881×10^{-5} sq cm/sec, using the formula $\frac{D_1}{D_2} = \frac{\sqrt{M_2}}{\sqrt{M_1}}$ [16].

Two waves are observed simultaneously when the indicated compounds are polarographed in solutions with a pH between 6.5 and 8, the sum of whose heights is approximately equal to the height of the wave in either alkaline or acid medium.

Besides the first wave, a second wave is also observed in unbuffered solutions with pH < 6, corresponding to the wave obtained in buffer solutions with pH > 8.

The appearance of this second wave is associated with a pH change in the layer of solution around the cathode due to consumption of H^+ ions during the reduction of the aminoacetophenone for the reaction corresponding to the first wave. Here the value of the pH in the layer around the cathode shifts toward higher values, and part of the aminoacetophenone molecule is reduced by the mechanism that prevails in an alkaline medium. For this reason the total height of these two waves is approximately equal to the height of the aminoacetophenone wave in the same concentration of solution in either acid or alkaline medium (for the meta and para isomers); for o-aminoacetophenone, as was to be expected from the data given in Table 2, the sum of the heights of the two waves is slightly less than the height of the first wave (appearing in the acid region) and slightly greater than the height of the second wave (Fig. 4).

The scheme for the reduction of the aminoacetophenones can be depicted in the following manner:

in acid medium

$$NH_2C_6H_4COCH_3 + 2H^+ + 2e \longrightarrow NH_2C_6H_4CHOHCH_3, \quad (1)$$

in alkaline medium

$$NH_2C_6H_4COHCH_2 + 2H_2O + 2e \longrightarrow NH_2C_6H_4CHOHCH_3 \quad (2)$$

When the aminoacetophenones are reduced in alkaline medium the hydrogen ions do not take a direct part in the reaction, and consequently the half-wave potential does not depend on the pH.

Since the amino group is an electron-donor group and, being found in either the ortho or para position, increases the electron density in the carbonyl group when compared with the same group in unsubstituted acetophenone, then the reduction of the o- and p-aminoacetophenones in alkaline medium proceeds at more negative potentials than in the case of acetophenone. In the case of m-aminoacetophenone such an electromeric shift of electrons to the CO group is not observed, and consequently the half-wave potential of the meta isomer is close to the $E_{1/2}$ of acetophenone. Holleck and Marsen observed a similar situation when they investigated the reduction of the carbonyl group found in various substituted benzaldehyde derivatives [13].

In acid medium, where the amines are found present as salts, i.e., the nitrogen of the amino group is positively charged (the NH_2 group migrates to NH_3^+ due to the addition of a proton), the tying up of the unshared pair of electrons of the amino group makes it impossible for the p-electrons of this group to couple with the π-electrons of the benzene ring. For this reason all of the aminoacetophenones in acid medium are reduced at potentials lying close to the reduction potential of acetophenone (at pH 2.2, $E_{1/2} = -1.08$ v). A slight divergence in $E_{1/2}$ for the various isomers in acid medium is apparently due only to their variable adsorption at a dropping-mercury cathode.

As regards the differences in the constants of the diffusion current in acid and in alkaline medium, then these differences appear only for the ortho isomer, in which the presence of intramolecular hydrogen-bonding between the CH group and the amino group makes a part of the molecule in alkaline medium incapable of being reduced in the investigated range of potentials. For the other isomers, as had been shown earlier, the constants of the diffusion current are the same in both the alkaline and acid regions.

This explanation of the differences in the behavior of the aminoacetophenones in acid and alkaline media is supported by the spectrographic data obtained by us: on acidification the absorption region of aqueous solutions of the aminoacetophenones shifts toward shorter wavelengths down to the absorption of acetophenone itself. In a similar manner, aniline in HCl gives the spectrum of benzene, nitroaniline gives the spectrum of nitrobenzene [14], and diphenylamine gives the spectrum of diphenyl [15].

Joint Polarographing of Aminoacetophenones

When m- and p- mixtures, and also m- and o-aminoacetophenone mixtures, are jointly polarographed in either unbuffered neutral media or in alkaline buffer solutions they give two separate waves that are situated quite close to each other – the half-wave potentials differ by 0.18 v for each of the indicated pair of isomers. The joint polarograms for the p- and m-aminoacetophenones are shown in Fig. 8. In acid solutions the waves of the isomers tend to merge, so that the values of $E_{1/2}$ for all three isomers nearly coincide. The total height of the waves of both isomers at pH 6.22 (unbuffered solution), and also at pH 10.7, is slightly less than the sum of the heights of the waves of the isomers, each taken separately, and found in a solution of the same concentration. Both the first and second waves of the ortho and para isomers merge at all pH values of the background. The height of the total wave of the ortho and para isomer is also less than the sum of their heights, each taken separately, and found in the same concentrations.

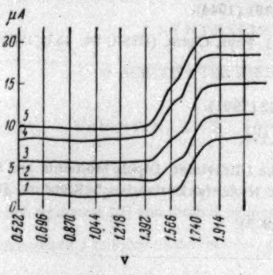

Fig. 8. Polarographic waves of a solution containing 1.34 mmoles/liter of p-aminoacetophenone (A) and various amounts of m-aminoacetophenone (B) in their joint presence with a background of 0.1 N Li_2SO_4.
1) A, 2) A + 0.335 mmoles/liter B, 3) A + 0.670 mmoles/liter B, 4) A + + 1.005 mmoles/liter B, 5) A + 1.340 mmoles/liter B.

As a result, for reasons as yet unknown to us, the isomers when mixed exert a mutual reducing effect on the heights of each other's waves. A similar phenomenon was observed by Adkins and Cox [3]: the height of the acetophenone wave was reduced when benzalacetone was added to the solution, however these authors also failed to give an explanation for the indicated facts.

SUMMARY

1. The characteristics of the polarographic behavior of the o-, m- and p-aminoacetophenones on a dropping-mercury cathode were investigated; here it was shown that they are all reduced in both buffered and unbuffered solutions.

2. The main polarographic constants: $E_{1/2}$, I_d and $\underline{n}$ of the above indicated isomers were determined. It was found that one wave is observed in the acid region (pH < 6.5), the $E_{1/2}$ of which is shifted toward negative potentials with increase in the pH. A second wave is observed in solutions with pH > 8, the $E_{1/2}$ of which remains constant with further change in the pH.

Two polarographic waves are observed for all of the isomers in the pH region 6.5-8.

3. It was shown that the position of the amino group in the aminoacetophenones exerts an influence on their polarographic activity: when in either the ortho or para position the amino group causes the reduction potential of the carbonyl group to shift to the negative side, while when the amino group is in the meta position it is practically without effect on the reduction potential.

4. The possibility of determining the isomeric aminoacetophenones in their joint presence was investigated.

In conclusion we wish to thank A. E. Lutsko for participating in a discussion of the results obtained in this study.

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Received March 14, 1957

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SYNTHESIS OF VINYL MONOMERS

I. α-SUBSTITUTED DERIVATIVES OF VINYLPHOSPHONIC ACID

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The known alkenylphosphonic acid derivatives include α-methylvinylphosphonic acid [1], diethyl α-carbomethoxyvinylphosphonate [2] and diethyl cyanovinylphosphonate [3].

We synthesized a number of derivatives, similar to those indicated above, by the method of oxidative phosphonation [4, 5].

The oxidation of a mixture of methyl acrylate and phosphorus trichloride with oxygen leads to the formation of chlorocarbomethoxyethanephosphonyl dichloride. Of the two isomers possible here, containing either the α-chloro-β-carbomethoxy or the β-chloro-α-carbomethoxy group, it is the latter that is formed. This was shown by converting the mentioned chloride to the diethyl ester, the dehydrochlorination of which with triethylamine gave the diethyl ester of α-carbomethoxyvinylphosphonic acid, identical with the above described [2]. The dimethyl ester of α-carbomethoxyvinylphosphonic acid is obtained in a similar manner. Relative to the properties of these esters it is interesting to mention that their reaction with ammonia under the usual conditions does not lead to the formation of amides.

Attempts to obtain the analogous α-chloro derivative of the vinylphosphonic acid, not reported in the literature, by the Pudovik method [6] from vinylidene chloride and dialkyl phosphite proved unsuccessful. In the presence of catalytic amounts of sodium methylate the reaction fails to go; with an equimolar amount of sodium methylate the formation of a small amount of trimethyl phosphate is observed.

Chlorocyanoethylphosphonic acid derivatives, the dehydrochlorination of which could yield cyanovinylphosphonic acid compounds, were synthesized by the oxidative phosphonation of vinyl cyanide. In this case, in contrast to methyl acrylate, the reaction is accompanied by the formation of two compounds, apparently representing the possible structural isomers of chlorocyanoethanephosphonyl dichloride. However, we were unable to separate these two chlorides by distillation. The separation of the isomers was achieved by converting the mixture of chlorides to the dimethyl esters. One of these esters proved to be a liquid, and the other was crystalline.

The liquid isomer when treated with triethylamine readily cleaves hydrogen chloride, forming the dimethyl ester of cyanovinylphosphonic acid; the position of the cyano group in this compound has not yet been established.

Attempts to synthesize the chlorocyanoethylphosphonic acid derivatives by the addition of phosphorus pentachloride to vinyl cyanide failed to give positive results; even at −15 to −20° the acrylonitrile undergoes chlorination with the formation of dichloropropionitrile.

The previously unknown dimethyl ester of vinylphosphonic acid was synthesized in the usual manner.

The esters of the substituted vinylphosphonic acid form polymers and copolymers with other vinyl monomers.

EXPERIMENTAL

β-Chloro-α-carbomethoxyethanephosphonyl Dichloride (I). Oxygen was passed through a mixture of 17 g of methyl acrylate and 137.5 g of phosphorus trichloride at 0° until reaction was complete. Then the phosphorus oxychloride was removed from the mixture by distillation. The residue was vacuum-distilled. We obtained 67.9 g (69.5%) of (I).

B. p. 124° (8 mm), d^{20}_4 1.5238; $n^{20}D$ 1.4745, MR_D 44.2; calc. 45.25.

Found %: C 20.03, 20.43; H 2.42, 2.51; P 12.93, 13.14. $C_4H_6O_3Cl_3P$. Calculated %: C 20.06; H 2.52; P 12.23.

Dimethyl β-Chloro-α-carbomethoxyethylphosphonate (II). With stirring and a temperature of about 0°, 23.9 g of (I) was gradually added to 100 ml of methanol. After removal of the excess methanol by distillation the residue was vacuum-distilled. We obtained 18 g (79%) of (II).

B.p. 130-132° (7 mm), d^{20}_4 1.3460, $n^{20}D$ 1.4428.

Found %: P 12.88, 13.48. $C_6H_{12}O_5ClP$. Calculated %: P 13.44.

Diethyl β-Chloro-α-carbomethoxyethylphosphonate (III). From 24 g of (I) and 100 ml of absolute ethanol, under the same conditions as described for the preparation of (II), we obtained 20.7 g (80%) of (III).

B.p. 153-155° (8 mm), d^{20}_4 1.2209, $n^{20}D$ 1.4329, MR_D 56.26; calc. 56.56.

Found %: P 11.81, 11.24. $C_8H_{16}O_5ClP$. Calculated %: P 11.90.

Dimethyl α-Carbomethoxyvinylphosphonate (IV). A solution of 23 g of (II) in 100 ml of dry ether was treated with 15.15 g of triethylamine. The next day the obtained precipitate was filtered, washed with ether, and the filtrate was fractionally distilled. We obtained 14.7 g (76%) of (IV).

B.p. 106° (2 mm), d^{20}_4 1.1268, $n^{20}D$ 1.4412, MR_D 40.5; calc. 41.9.

Found %: P 15.95, 15.20. $C_6H_{11}O_5P$. Calculated %: P 15.97.

Diethyl α-Carbomethoxyvinylphosphonate (V). From 25.85 g of (III) and 15.15 g of triethylamine, under the same conditions as described for the preparation of (IV), we obtained 16.5 g (75%) of (V).

B.p. 118-119° (3 mm), d^{20}_4 1.1621, $n^{20}D$ 1.4348, MR_D 49.8; calc. 51.2.

Found %: P 12.72, 12.91. $C_8H_{15}O_5P$. Calculated %: P 13.09.

Cyanochloroethanephosphonyl Dichloride (VI). Oxygen was passed through a mixture of 53 g of acrylonitrile and 344 g of phosphorus trichloride at 10-20° until reaction ceased. The formed phosphorus oxychloride was removed from the reaction mixture at 50° (50-60 mm). The residue was distilled at 2 mm. The following fractions were isolated: 1st, 50-95° (9 g), 2nd, 95-105° (60 g), and 3rd, residue (20 g).

Redistillation of the 2nd fraction gave 33.6 g (16.6%) of (VI).

B. p. 99-101° (2 mm), d^{20}_4 1.5721, $n^{20}D$ 1.4783, MR_D 38.5; calc. 38.8.

Found %: C 17.05, 17.21; H 2.22, 1.89; Cl (hydrolyzable) 34.28; N 6.67, 6.69; P 14.63, 15.26. $C_3H_3OCl_3NP$. Calculated %: C 17.43; H 1.44; Cl (hydrolyzable) 34.88; N 6.77; P 15.00.

Dimethyl Cyanochloroethylphosphonate (VII). With stirring and a temperature of about 0°, 30 g of (VI) was gradually added to 140 ml of methanol. The excess methanol was removed in vacuo. The residue, an only liquid mixed with crystals, was treated with dry ether. Here the oily liquid went into solution. After separation from the crystals, the solution was fractionally distilled. After 2 fractional distillations we obtained 5.8 g of (VII).

B. p. 134-135° (2 mm), d^{20}_4 1.3275, $n^{20}D$ 1.4403, MR_D 39.3; calc. 40.7.

Found %: C 31.2, 30.9; H 4.20, 3.80; Cl 17.68; 17.35; N 6.48, 6.24; P 15.44, 15.61. $C_5H_9O_3ClNP$. Calculated %: C 30.38; H 4.55; Cl 17.97; N 7.08; P 15.69.

The product is insoluble in water. The water extract does not give a test for chloride ion.

Treatment of the ether solution of the product with triethylamine gave a precipitate of triethylamine hydrochloride.

Dimethyl Cyanovinylphosphonate (VIII). From 8 g of (VII) and 8 g of triethylamine, under the same conditions as described for the preparation of (IV), we obtained 1.8 g of (VIII).

B. p. 95-96° (2 mm),* d^{20}_4 1.2458, $n^{20}D$ 1.4327.

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*From the amount of chlorine which was contained in the triethylamine hydrochloride precipitate it could be assumed that the dehydrochlorination had gone to the extent of 80%. However, considerable decomposition of the product occurred during distillation.

Found %: N 8.61, 8.92; P 18.98, 19.17. $C_5H_{18}O_3NP$. Calculated %: N 8.7; P 19.25.

Dimethyl Vinylphosphonate (IX). A solution of 18.5 g of potassium hydroxide in 120 ml of methanol was added in drops to 45 g of dimethyl β-chloroethylphosphonate. The mixture was heated on the water bath for one hour, and then allowed to stand overnight. The obtained precipitate of potassium chloride was filtered and washed with methanol. The methanol was distilled from the filtrate, and 36 g (80%) of (IX) was obtained from the residue.

B. p. 82-84° (3.5 mm), d^{20}_4 1.1696, $n^{20}D$ 1.4305, MR_D 30.58; calc. 31.17.

Found %: P 22.40, 22.27. $C_4H_9O_3P$. Calculated %: P 22.8.

SUMMARY

1. The oxidative phosphonation of methyl acrylate and acrylonitrile gave the corresponding chlorocarbomethoxy- and chlorocyanoethanephosphonyl dichlorides, and these treated with alcohols gave the corresponding esters.

2. Dehydrochlorination of the above mentioned esters led to obtaining cyano- and carboalkoxy-substituted vinylphosphonates.

Received April 25, 1957

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SYNTHESIS OF VINYL MONOMERS

II. SOME DERIVATIVES OF α-CHLOROACRYLIC ACID

A. Ia. Iakubovich, E. P. Pravova and N. A. Bogoslovskii

Many derivatives of α-chloroacrylic acid as yet remain unknown. The synthesis of some of these compounds is described below.

The previously unknown α-chloroacryloyl fluoride was obtained by us from the corresponding acid halides. The method of A. N. Nesmeianov and E. Kan [1] was used to obtain the indicated fluoride in 45% yield. Attempts to synthesize the fluoride by heating (160-170°) α-chloroacrylic acid with benzoyl fluoride or by the exchange reaction of α-chloroacryloyl chloride with potassium fluoride gave negative results. The α-chloroacryloyl chloride was obtained by us not by the dehydrochlorination of dichloropropionyl chloride [2], but instead directly from α-chloroacrylic acid. The best yield (40%) was obtained when the acid was reacted with benzoyl chloride; the yields of α-chloroacryloyl chloride were lower when other acid chlorides (PCl_3, $SOCl_2$, $C_6H_5CCl_3$) were used.

Using the α-chloroacryloyl chloride, we synthesized by conventional procedures the p-cyclohexylphenyl ester (new), N-phenylamide (new) and ethyl ester of α-chloroacrylic acid. In its properties the ethyl α-chloroacrylate failed to differ from the previously described ester [2-4], and was obtained by us by the direct esterification of α-chloroacrylic acid with ethanol. The mentioned α-chloroacrylic acid derivatives are capable of giving polymers and copolymers with vinyl monomers.

EXPERIMENTAL

α-Chloroacryloyl Fluoride (I). A mixture of 128 g of benzoyl chloride, 58 g of fused potassium fluoride powder and about 30 g of α-chloroacrylic acid was charged into a round-bottomed flask, fitted with thermometer, a Vigreux column with a height of 10-15 cm, condenser, and a receiver, cooled in ice and protected by a calcium chloride tube. The mixture was heated to 80-90°, where a stormy reaction began, and (I) began to distill; another 23 g of α-chloroacrylic acid was added in portions (4-5 g) when the distillation began to slow up. At the end the bath temperature was raised to 150°, and the distillate up to 130° collected. Redistillation of the distillate gave 27 g of (I) with b.p. 67-67.5°.. Yield 45%. The substance is a clear, colorless liquid that fumes in the air, and whose vapors irritate the mucous membranes; the substance etches glass when stored in it.

Found %: Cl 31.5; F 16.8. C_3H_2OClF. Calculated %: Cl 32.7; F 17.51.

α-Chloroacryloyl Chloride (II). a) A mixture of 205 g of benzoyl chloride, 78 g of α-chloroacrylic acid, 5.66 g of cuprous chloride and 2.83 g of hydroquinone was charged into a Claisen flask, fitted with a descending condenser and receiver. Vacuum was applied to the system (residual pressure 76 mm), and the flask contents were gradually heated on the water bath to 80°. The acid chloride formed here was distilled off (vapor temperature 45-69°). The yield of crude acid chloride obtained in this manner was 48.5 g. Redistillation gave 35.5 g (39%) of (II) as a clear, colorless liquid that fumed in the air and had a very sharp lachrymatory odor. B. p. 46-47° (76 mm), $n^{20}D$ 1.4720, d^{20}_{20} 1.3628.

b) A mixture of 5 g of α-chloroacrylic acid, 9.2 g of benzotrichloride, 0.47 g of cuprous chloride and 0.2 g of fused zinc chloride was heated in a flask under reflux at 70-75°. Heating was continued until hydrogen chloride ceased to evolve. Vacuum-distillation of the reaction mixture gave 1.6 g of (II) with b.p. 46-47° (76 mm). Yield 27%.

c) A solution of α-chloroacrylic acid in methanol was neutralized with the calculated amount of a 10 % sodium methylate solution in methanol. Here the sodium salt separated as a white crystalline precipitate; the remainder of the salt was obtained when the solution was evaporated in vacuo. A mixture of 5 g of sodium α-chloroacrylate, 9.26 g of thionyl chloride and 0.22 g of cuprous chloride was heated at 70-80° for 45 minutes. The excess thionyl chloride was distilled off and the residue was vacuum-distilled. We obtained 1.7 g (38%) of (II) with b.p. 46.5-47° (76 mm).

N-Chloroacrylanilide (III). A 10% solution of 1.5 g of aniline in benzene was added to a 10% benzene solution of 1 g of (II). In 10-15 minutes the precipitate of aniline hydrochloride was filtered, and the filtrate was evaporated in vacuo. The residue (1.2 g) was recrystallized from aqueous alcohol to give 1 g of pure (III) as colorless crystals (m.p. 52.5-53.5°), insoluble in water, and readily soluble in the common organic solvents.

Found %: C 59.9; H 4.26; N 7.23. C_9H_8ONCl. Calculated %: C 59.5; H 4.4; N 7.71.

p-Cyclohexylphenyl α-Chloroacrylate (IV). The starting p-cyclohexylphenol was synthesized by the Meyer and Bernhauer method [5]. We obtained a melting point of 122-123° (instead of the indicated 131-132°). The yield was several percent of the theoretical (based on cyclohexanol).

A suspension of 3 g of dry sodium p-cyclohexylphenate in 20 ml of benzene was treated with a solution of 2.4 g of (II) in 10 ml of benzene. The reaction mixture was heated at 75° for 1.5 hours, cooled, and filtered. Evaporation of the filtrate gave 3.1 g of residue. After 2 recrystallizations of the residue from alcohol, and then from petroleum ether, we obtained 0.8 g of pure (IV) as colorless crystals with m.p. 62.5-63.5°. The substance is readily soluble in organic solvents, and insoluble in water. Yield 20%.

Found %: C 67.29; H 6.96; Cl 11.63. $C_{15}H_{17}O_2Cl$. Calculated %: C 68.0; H 6.45; Cl 13.5.

Ethyl α-Chloroacrylate (V). a) To 35.6 g of absolute ethyl alcohol was added in drops 21 g of (II) at 50-55°, after which the mixture was heated at 100° until HCl was no longer evolved, and then it was vacuum-distilled, having added antioxidant (N-phenyl-2-naphthylamine). We obtained 6-6.5 g of (V) with b.p. 52.5-53.5° (18 mm), $n^{20}D$ 1.4384.

b) A mixture of 10.7 g of α-chloroacrylic acid, 9.2 g of absolute ethyl alcohol and 0.8 ml of concentrated sulfuric acid was heated under reflux for 3 hours, then the mixture was neutralized with soda, filtered, and vacuum-distilled. We obtained 3.6 g of (V) with b.p. 43-45° (15 mm), $n^{20}D$ 1.4384.

SUMMARY

The syntheses of the acid fluoride, the acid chloride and some of the previously unknown derivatives of α-chloroacrylic acid were described.

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Received April 25, 1957

DECARBOXYLATION OF ACRIDINE-9-CARBOXYLIC ACIDS WITH CARBONYL-CONTAINING COMPOUNDS

A. I. Gurevich

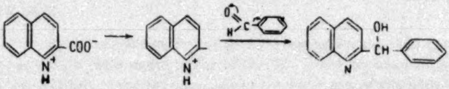
Secondary reactions accompanying the decarboxylation of heterocyclic carboxylic acids in a solvent have been little studied. Dyson and Hammick [1] observed that quinaldinic and isoquinaldinic acids dissolved in aromatic aldehydes and ketones form the corresponding carbinols or ketones on decarboxylation as a result of condensation. In later reports by Hammick and coworkers [2-6] and Mislow [7] the range of the reaction was extended. It was established that picolinic, isonicotinic, and cinchoninic acids undergo analogous transformations and that the second component in the condensation may be quinoline, dinitrobenzene, dinitrochlorobenzene, or an ester of an aromatic or aliphatic-aromatic acid. It was also established that the decarboxylation of quinaldinic [5] and picolinic [8] acids is a first-order reaction. It was suggested that the acids being decarboxylated exist in the form of zwitter-ions, and that the carbanion formed on decarboxylation reacts like the CN ion.

In the present report analogous reactions of acridine-9-carboxylic acid are studied. The acids were decarboxylated in various aldehydes and ketones and in ethyl p-nitrobenzoate at a temperature of the order of 200° in a nitrogen stream (in order to avert oxidation of possible reaction products by atmospheric oxygen).

As a result of the reaction of acridine-9 carboxylic acids with the appropriate aldehydes we obtained 9-benzoyl-, 9-o-chlorobenzoyl-, and 9-p-nitrobenzoylacridines, as well as 2-methoxy-6-chloro-9-(p-nitrobenzoyl)acridine. The yield was about 30% in all cases. The synthesized substances do not form the usual ketone derivatives (phenylhydrazones, thiosemicarbazones), and the presence of the ketone function in these compounds is assumed on the basis of the absence of active hydrogen atoms.

We attempted to carry out the analogous reactions of acridine-9-carboxylic acid with benzophenone and p-nitroacetophenone, as well as those of 2-methoxy-6-chloroacridine-9-carboxylic acid with 1-diethylaminopentanone-4 and ethyl p-nitrobenzoate. In all cases only the corresponding acridines, unsubstituted in position 9, were isolated; yields were 44, 87, 64 and 18%, respectively. Condensation with ketones and carboxylic acid esters, unlike analogous reactions in the pyridine and quinoline series, is probably impossible owing to the steric inaccessibility of the carbonyl carbon atom to the acridine radical.

We noticed that while decarboxylation of 2-methoxy-6-chloroacridine-9-carboxylic acid in the solvent p-nitrobenzaldehyde proceeds relatively slowly even at a temperature of the order of 200°, decarboxylation in the solvents p-dimethylaminobenzaldehyde and 1-diethylaminopentanone-4 goes rapidly even at 80-100°. This undoubtedly contradicts the assertion of Hammick et al. [5] that the activation energy of the decarboxylation reaction does not depend on the solvent. In the last two cases an ionic reaction mechanism should undoubtedly be assumed. However, we were unable to isolate the product of condensation with p-dimethylaminobenzaldehyde (only 2-methoxy-6-chloroacridine was isolated, with a yield of 66%), which creates doubt as to the correctness of the scheme with an ionic reaction mechanism, proposed by Brown and Hammick [4].

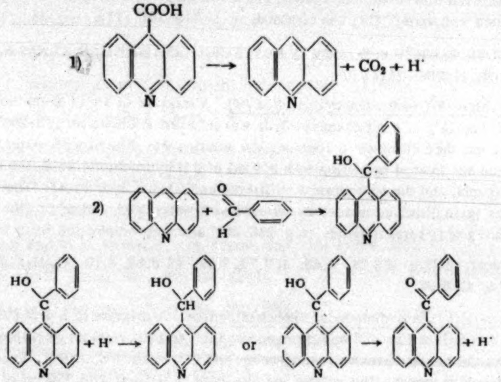


The fact that in our experiments substituents in the ring of the aldehyde were found to have no substantial effect on the yield of the condensation product also fails to conform to this scheme.

Furthermore, the Brown-Hammick scheme does not explain the fact that in a number [illegible] the reaction products are not carbinols but ketones. It does not seem very likely that these carbinols could easily be oxidized in an aldehyde medium and a nitrogen atmosphere.

We attempted to synthesize such carbinols in the acridine series since in our decarboxylation experiments we always obtained only ketones, and, according to Brown [6], it was to be expected that these carbinols would be very easily oxidized in air to the corresponding ketones. We were unable to reduce either 9-(o-chlorobenzoyl)acridine or 9-(p-nitrobenzoyl)acridine by prolonged heating at 80° with aluminum isopropoxide in isopropyl alcohol. We hydrogenated 9-benzoylacridine in alcohol over Raney nickel. On oxidation of the (9,10-dihydroacridyl-9)-phenylcarbinol thus obtained with ferric chloride in hydrochloric acid solution, acridine was isolated with an 80% yield. Oxidation of the dihydroacridylphenylcarbinol by air led to (acridyl-9)-phenylcarbinol but not to 9-benzoylacridine, which would necessarily have resulted if (acridyl-9)-phenylcarbinol had been easily oxidized by air.

The noted facts may be explained by assuming that decarboxylation accompanied by condensation of the heterocyclic radical with the solvent is accomplished by the radical mechanism



In conclusion I express my thanks to A. M. Grigorovskii for his valuable advice, which made possible the completion of the present work.

EXPERIMENTAL

9-Benzoylacridine (I). A mixture of 2 g of acridine-9-carboxylic acid (II) and 50 ml of benzaldehyde was refluxed 5 hours at 160-165° in a nitrogen stream. Excess benzaldehyde was distilled in vacuo from the homogeneous mixture obtained. The residue was diluted with 50 ml of ether. The ether evaporated on long standing, and after this the residue contained a crystalline substance. The crystals were filtered, washed with ether, and dried in a vacuum-desiccator. The yield of (I) was 0.8 g (29.6%). M.p. 216-217° after recrystallization from alcohol [9, 10].

Found %: C 80.25, 80.40; H 4.76, 4.77; N 4.74; H_2O 4.50. $C_{20}H_{13}ON \cdot H_2O$. Calculated %: C 79.73; H 4.98; N 4.65; H_2O 5.98.

Hydrochloride: m.p. 228-234° (from 2 N hydrochloric acid).

Found %: Cl 11.00. $C_{20}H_{14}ONCl$. Calculated %: Cl 11.11.

9-(o-Chlorobenzoyl)acridine (III). A mixture of 7 g of (II) and 44 g of o-chlorobenzaldehyde was refluxed 5 hours at 175-185° in a nitrogen stream. Excess o-chlorobenzaldehyde was distilled in vacuo from the homogeneous mixture obtained. The residue was diluted with 300 ml of ether. Without removing the slight suspended precipitate the ethereal solution was saturated with hydrogen chloride. The precipitated hydrochloride mixture was filtered, washed with ether, and dried in a vacuum-desiccator. The dried hydrochloride mixture was heated to boiling with 300 ml of water acidified with 0.5 ml of concentrated hydrochloric acid, 7 g of sodium sulfite was added, the mixture was boiled 5 minutes, and the hot solution was filtered and made alkaline with caustic soda. The yield was 1.85-2.00 g of acridine (32.9-35.6%) with a m.p. of 105-107°. The residue which did not dissolve in water on treatment of the hydrochlorides with sodium sulfite was twice recrystallized from 70% acetone; (III) was obtained. The aqueous-acetone mother liquor was concentrated, and the precipitated (III) was again recrystallized. Total yield, 2.6-2.9 g (26.0-29.0%). M.p. 182-183°.

Found %: C 75.09; H 3.89; N 4.65, 4.75; Cl 10.87, 11.16. $C_{20}H_{12}ONCl$. Calculated %: C 75.59; H 3.78; N 4.41; Cl 11.18.

Hydrochloride: m.p. 255-256° (from 2 N hydrochloric acid).

9-(p-Nitrobenzoyl)acridine (IV). A mixture of 2 g of (II) and 11.5 g of p-nitrobenzaldehyde was refluxed one hour at 170-190° in a nitrogen stream. The reaction mixture was then treated by boiling with 750 ml of 2 N hydrochloric acid, and the solution was separated from the oil. The precipitate which settled out of the solution on cooling was filtered and washed with acetone. The yield of hydrochloride (IV) was 0.7 g (21.4%). The hydrochloride was dissolved in a mixture of acetone and a few drops of concentrated ammonia, and the solution was filtered and diluted with water. (IV) was obtained; m.p. 219-221° [11].

Found %: C 69.91, 70.07; H 4.05, 4.00; N 8.36, 8.49; H_2O 4.48. $C_{20}H_{12}O_3N_2 \cdot H_2O$. Calculated %: C 69.37; H 4.04; N 8.09; H_2O 5.20.

2-Methoxy-6-chloro-9-(p-nitrobenzoyl)acridine (V). A mixture of 3 g of 2-methoxy-6-chloroacridine-9--carboxylic acid (VI) and 15 g of p-nitrobenzaldehyde was refluxed 1.5 hours at 190-200° in a nitrogen stream. The reaction mixture was then dissolved in acetone; the solution was diluted with water. The precipitate which settled out was filtered and treated by boiling with 300 ml of 2 N hydrochloric acid, the solution was filtered and neutralized with ammonia, and the precipitate was filtered and washed with water. The residue undissolved in hydrochloric acid was again dissolved in acetone, diluted with water, and worked up like the preceding. After repeated treatment 1.3 g of (V) was isolated; m.p. 236-238° after reprecipitation from acetone by water.

Found %: C 64.61, 64.38; H 3.74, 3.48; N 7.70, 7.89; Cl 8.88, 8.70. $C_{21}H_{13}O_4N_2Cl$. Calculated %: C 64.20; H 3.31; N 7.14; Cl 9.04.

Decarboxylation of (VI) in p-dimethylaminobenzaldehyde. A mixture of 5 g of (VI) and 20 g of p-dimethylaminobenzaldehyde was refluxed at 200° in a nitrogen stream. At 100° vigorous decarboxylation had already begun; after 15 minutes the mixture became homogeneous and CO_2 evolution ceased. Excess p-dimethylaminobenzaldehyde was distilled off in vacuo. The residue was dissolved by boiling with 750 ml of 0.2 N hydrochloric acid, the solution was filtered, and to it was added 75 ml of concentrated hydrochloric acid; the precipitate which settled out on cooling consisted of 2-methoxy-6-chloroacridine hydrochloride. Yield, 2.8 g (66.1%); m.p. 243-245°. 2-Methoxy-6-chloroacridine was precipitated from an aqueous solution of the hydrochloride with ammonia and recrystallized from aqueous acetone. M.p. 181-182° [12].

Found %: C 69.27, 69.23; H 4.50, 4.40; N 5.33; Cl 14.13. $C_{14}H_{10}ONCl$. Calculated %: C 69.54; H 4.11; N 5.75; Cl 14.61.

(9,10-Dihydroacridyl-9)phenylcarbinol (VII). Hydrogenation of 0.5 g of (I) in 60 ml of alcohol was accomplished over 0.5 g of Raney Ni in the course of 5 hours at 50°; the mixture was cooled and filtered, the filtrate concentrated in vacuo to 20 ml, and the residue diluted with water. The precipitate which separated out was filtered and dried in a vacuum-desiccator. The yield of (VII) was 0.32 g; m.p. 204-205° after recrystallization from alcohol.

Found %: C 83.58; 83.42; H 6.24, 6.17; N 4.75, 5.13. $H_{act.}$ 1.16, 1.35. $C_{20}H_{17}ON$.
Calculated %: C 83.62; H 5.92; N 4.88; $H_{act.}$ 0.70.

(Acridyl-9)phenylcarbinol (VIII). Air was blown through a solution of 0.1 g of (VII) in 40 ml of alcohol at 50° for 5 hours. The alcohol was evaporated in vacuo, and 0.09 g of (VIII) was obtained; m.p. 189-191° after recrystallization from alcohol. Melting point of a sample mixed with (VII), 182-185°. Melting point of a sample mixed with (I), 180-185°.

Found %: $H_{act.}$ 0.40. $C_{20}H_{15}ON$. Calculated %: $H_{act.}$ 0.35.

SUMMARY

1. The decarboxylation of acridine-9-carboxylic acids dissolved in carbonyl-containing compounds has been studied. It has been shown that 9-benzoylacrdine derivatives are formed by secondary reaction with the aldehydes. In ketones and carboxylic-acid esters secondary reactions are not observed, probably owing to steric hindrance.

2. The ionic reaction mechanism proposed earlier does not explain certain discovered facts.

3. A scheme with a radical reaction mechanism is proposed.

Received January 30, 1957

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ON THE PRODUCTS FORMED IN THE CONDENSATION OF n-BUTANOL IN THE PRESENCE OF SODIUM BUTOXIDE AND A COPPER CATALYST

V. I. Liubomilov and E. T. Belianina

In the production of 2-ethylhexanol by the condensation of n-butanol in the presence of sodium butoxide and a dehydrogenating catalyst [1], the hydrogen evolved in the reaction has the odor of butyraldehyde. This aldehyde was proved by preparing the 2,4-dinitrophenylhydrazone. Further, on separation of the reaction products it was found that the 180-185° fraction corresponding to 2-ethylhexanol-1 contains an unsaturated compound which is characterized by its bromine number. From this fraction we isolated the unsaturated alcohol 2-ethylhexenol-1, identical to the unsaturated alcohol obtained by Braun and Manz [2] by dehydration of octylene glycol [octoglycol] ether. To this alcohol they ascribe the structure of α-ethyl-β-n-propylallyl alcohol. Acid products were isolated from the sodium salts formed in the condensation of n-butanol and were studied. Besides butyric and 2-ethylcaproic acids [3], the lactone $C_{12}H_{22}O_2$ was also isolated.

EXPERIMENTAL

Condensation of n-butanol. A flask with a stirrer, reflux condenser, and thermometer was charged with 300 g of n-butanol, and 32 g of metallic sodium was dissolved in the latter. The flask was heated in an oil bath to 125-130°, and into it was put 0.6 g of basic copper carbonate catalyst* previously dried in an oven at 120-130°. Evolution of hydrogen began in 20-30 minutes. The reaction was continued for 10-12 hours, until hydrogen evolution had almost entirely ceased. The reaction product was steam distilled. The residue in the flask, which consisted of an aqueous solution of sodium salts, was filtered to remove the catalyst, concentrated by evaporation, and acidified with 42 ml of 90% sulfuric acid. The organic acids separated out in the form of an oily layer.

Yields and Properties of Products Isolated from Salts

Products	Yield (in g)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Acid number	
					found	calculated
Butyric acids	412.7	161—162° (737), 105—108 (80)	0.9585	1.3992	633	637
2-Ethylcaproic acid	128.6	227—228 (750), 113—114 (7.5)	0.9118	1.4274	384	389
Lactone*	71.7	132—134 (7.5)	0.9642	1.4622	0	0

* The properties are given for a product washed in soda solution and water, and redistilled.

Proof of the presence of butyraldehyde. The hydrogen was passed through a bottle containing a saturated alcoholic solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazone was obtained in the form of long, yellow needles, m.p. 121.5-122° (from alcohol). Literature data [4]: m.p. 122-123°.

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* The authors express their cordial thanks to B. M. Dubinin, who recommended the use of this catalyst.

2-Ethylhexenol-1. The steam-distilled products were separated from the water and rectified. After repeated rectification of the intermediate fractions there were obtained: 38.0 g of n-butanol, 103.5 g of the 180-185° fraction, and 13.5 g of still residue. The bromine number of the 180-185° fraction was 32.5. From a series of experiments conducted under similar conditions several kilograms of the 180-185° fraction was obtained. By means of a series of successive rectifications of the latter in vacuo with a column having an efficiency of about 20 theoretical plates, we were able to obtain a small quantity of a substance, the properties of which did not change on subsequent rectification:

b.p. 177.5-178.5° (760 mm), b.p. 60° (9 mm), d^{20}_4 0.8427, $n^{20}D$ 1.4428.

Found %: OH 13.6. Bromine number 1254, 1248. $C_8H_{15}OH$. Calculated %: OH 13.3. Bromine number 1248.

Literature data [2]: b.p. 68-71°(12 mm), d^{22}_4 0.8414, $n^{22}D$ 1.4418.

2-Ethylhexanol-1 was obtained in pure form by hydrogenation of the 180-185° fraction or by treatment of the latter with an aqueous potassium permanganate solution, steam distillation, and rectification:

b.p. 183-184°, d^{20}_4 0.8325, $n^{20}D$ 1.4325; bromine number 0.

Note that on careful rectification of the 180-185° fraction the end fractions had higher bromine numbers than the middle ones. This indicated the possible presence of a second isomer of 2-ethylhexenol-1.

Investigation of acid products. The 700-g quantity of acid products accumulated from a series of experiments was rectified in vacuo. The yields and properties of the fractions obtained are given in the table.

The fraction with an acid number of 0 was a colorless liquid, more viscous than the preceding fractions, insoluble in water, and soluble in organic solvents. On treatment of this fraction by slight heating with 2% aqueous alkali it gradually dissolved, but on acidification with sulfuric acid it separated out unchanged.

Found %: C 71.80; H 11.24. Ester number 271. $C_{12}H_{22}O_2$. Calculated %: C 72.67; H 11.19. Ester number 282.

SUMMARY

In the condensationof n-butanol in the presence of sodium butoxide, besides 2-ethylhexanol-1, 2-ethylhexenol-1 is formed. Besides butyric and 2-ethylcaproic acids, the lactone $C_{12}H_{22}O_2$ was isolated from the carboxylic acid salts.

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Received February 4, 1957

REACTION OF BUTYRALDEHYDE WITH A SOLUTION OF SODIUM BUTOXIDE IN n-BUTANOL

V. I. Liubomilov

The condensation of n-butanol in the presence of its sodium alcoholate and a catalyst [1] leads to the formation, together with 2-ethylhexanol-1, of the corresponding unsaturated alcohol. In connection with the preceding reports [2, 3] it was of interest to make sure of the formation of the stated alcohols in the reaction of butyraldehyde with a solution of sodium butoxide in n-butanol. They were indeed prepared and isolated in this reaction. In the fraction corresponding to a mixture of 2-ethylhexanol-1 with unsaturated alcohols there are probably two isomers of 2-ethylhexenol-1, one of which was isolated in pure form and proved to be identical with the alcohol isolated from the product of n-butanol condensation [1]. Of the properties of this isomer, its ability to isomerize to 2-ethylhexanal-1 on passing over an incandescent silver wire should be noted.

EXPERIMENTAL

Reaction of butyraldehyde with a solution of sodium butoxide in n-butanol. A flask with a stirrer, reflux condenser, thermometer, and dropping funnel was charged with a weighed portion of n-butanol, and a weighed portion of metallic sodium was dissolved in the latter. The flask was heated in an oil bath, and a weighed portion of butyraldehyde was trickled into it from a dropping funnel during a fixed time interval. Then the flask was cooled, the reaction product steam-distilled, the distilled alcohols redistilled with a herringbone fractionating column 20 cm high, and the fraction with the boiling range 175-182° was separated out. The results of the experiments are given in the table.

Condensation of Butyraldehyde with a Solution of Sodium Butoxide in n-Butanol

Charge (in g)			temp.	Addition time of aldehyde (in hours)	Yield of 175 -182° fraction (in g)	Bromine numbers of 175-182° fraction
n-butanol	sodium	butyraldehyde				
80	8	26	70°	0.5	0	—
80	8	26	100	0.5	4.1	792
80	8	26	110	0.5	9.72	876
80	8	26	130	0.5	14.15	804
80	9.9	26	140	0.5	14.05	852
80	9.9	26	110	0.5	10.8	845
80	4.0	26	110	0.5	3.45	788
80	8	19.4	130	0.5	9.50	818
80	8	38.8	130	1.0	12.1	777
320	32	104	130	2.5	54.5	729
1600	160	520	130	6.0	344.2	513
80	8	26	130	5.0	14.5	615

First isomer of 2-ethylhexenol-1. On slow rectification of the 175-182° fraction in vacuo with a column of about 20 theoretical plates, fractions with high bromine numbers (over 1000) were obtained. Repeated rectification permitted the isolation of a substance with the following properties:

b.p. 177-178° (755 mm), b.p. 70-71° (12 mm), d^{20}_4 0.8418, $n^{20}D$ 1.4438.

Found %: C 74.07; H 12.72; OH 13.8. Bromine number 1215. $C_8H_{15}OH$. Calculated %: C 74.94; H 12.58; OH 13.3 Bromine number 1248.

The stated properties are similar to those of 2-ethylhexenol-1, described earlier [1].

The catalytic oxidation of 2-ethylhexenol-1 by air over an incandescent silver wire was attempted. However, it turned out that 2-ethylhexenol-1 in this case easily isomerizes to 2-ethylhexanal. Thus, a single passage of 2--ethylhexenol-1 vapor and air over an incandescent silver wire gave a condensate with an aldehyde content of 42%, calculated as 2-ethylhexanal (by the hydroxylamine method). Treatment of a sample of this condensate with an alcoholic solution of 2,4-dinitrophenylhydrazine gave the 2,4-dinitrophenylhydrazone in the form of yellow needles with m.p. 120.5-121.5° (from alcohol). A sample mixed with 2-ethylhexanal 2,4-dinitrophenylhydrazone did not give a melting-point depression. The dimedon derivative, obtained in aqueous alcohol in the form of long, white needles, had m.p. 191-191.5° (from 50% alcohol), and a sample mixed with the corresponding 2-ethylhexanal derivative did not give a melting-point depression, either.

2-Ethylhexanol-1. For the removal of unsaturated alcohols the 175-182° fraction was treated with a dilute aqueous potassium permanganate solution. On subsequent steam distillation followed by distillation of the alcohol layer which had separated out in the condensate, a product with the following properties was obtained:

b.p. 182-184°, d^{20}_4 0.8325, $n^{20}D$ 1.4325, bromine number 0.

Found %: C 73.31; H 14.07; OH 13.2. $C_8H_{17}OH$. Calculated %: C 73.79; H 13.93; OH 13.1.

On the second isomer of the unsaturated alcohol. In the fractionation of the 175-182° fraction in vacuo with the above-mentioned column, after the separation of fractions of the first isomer of 2-ethylhexenol-1 the bromine numbers of the fractions gradually decreased to 552. Then, as the boiling point rose very slightly, the bromine numbers of the fractions again increased, reaching 752. The last fraction boiled off at 183-185° (752 mm) ($n^{20}D$ 1.4440). A weighed portion of the latter (2.2 g) was hydrogenated with a Raney-nickel catalyst in an ethyl alcohol solution. The amount of H_2 absorbed was 233 ml (S.T.P.). After distillation, the substance obtained had a b.p. of 182-184°, d^{20}_4 0.8320, $n^{20}D$ 1.4322, which corresponds to the constants of 2-ethylhexanol-1.

SUMMARY

The reaction of butyraldehyde with a solution of sodium butoxide in n-butanol has been investigated. It has been shown that in this case two isomers of 2-ethylhexenol-1 are formed, one of which was isolated and proved to be identical with the alcohol isolated earlier from the products of n-butanol condensation.

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Received February 4, 1957

Scientific Research and Project
Institute of Plastics

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*Original Russian pagination. See C. B. Translation.

EFFECT OF NUCLEOPHILICITY OF THE ANION ON THE CHARACTER OF BONDING IN COMPOUNDS OF TROPYLIUM

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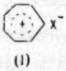
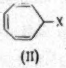
In recent years a number of salts of the aromatic seven-membered cycloheptatrienylium (tropylium) cation (I) have been obtained [1-3]. All of them are salts of quite strong acids [$X = Cl, Br, I, ClO_4, PtCl_6, B(C_6H_5)_4, NCO$].



(I)



(II)

On the other hand, tropylium oxide, methoxytropylium, tropylium cyanide and tropylium sulfide [1, 2] where X^- is the anion of quite a weak acid, are covalent compounds of the (II) type.*

It is evident that the character of the bond between the cycloheptatrienylium radical C_7H_7 and X depends on the nucleophilicity of the X^- anion. It could be expected that the greater the nucleophilicity of X^-, the smaller its tendency to cleave with a pair of electrons and the more covalent should be the C_7H_7-X bond.

An examination of the dissociation constants of the corresponding HX acids (which can serve as a measure of the nucleophilicity of the X^- anion) reveals that an extremely weak acid, forming ionic salts with tropylium, is HNCO ($K_a = 1.2 \cdot 10^{-4}$); an extremely strong acid, of the acids giving covalent compounds with tropylium, is HCN ($K_a = 7.2 \cdot 10^{-10}$).

Our problem was to find the boundary where the transition from the ionic bond $C_7H_7^+X^-$ to the covalent bond C_7H_7-X occurs. For this we synthesized the tropylium derivatives of acetic and benzoic acids ($K_a = 1.75 \cdot 10^{-5}$ and $6.3 \cdot 10^{-5}$).

Both the tropylium acetate and benzoate (more accurately cycloheptatrienyl acetate and benzoate) proved to be typical covalent compounds, i.e., liquids, soluble in nonpolar solvents. The covalent character of the C_7H_7-X bond in tropylium acetate is also supported by its ultraviolet absorption spectrum (λ_{max} 224 and 298 mμ; log ε 4.20 and 3.58), which is different from the spectra of tropylium salts (λ_{max} = 275 mμ, log ε 3.64).

As a result, the transition from ionic salts of tropylium to the covalent derivatives lies in the K_a interval for the corresponding acids of $1.2 \cdot 10^{-4}$ (HNCO) to $6.3\text{-}1.75 \cdot 10^{-5}$ (C_6H_5COOH and CH_3COOH). These results agree with the data of Doering [1] that the tropylium ion in water behaves like an acid with $K_a = 1.8 \cdot 10^{-5}$, reacting according to the scheme

$$C_7H_7^+ + 2H_2O \longrightarrow C_7H_7OH + H_3O^+.$$

The obtained data permit the conclusion that acids with $K_a \geq 1.2 \cdot 10^{-4}$ will give ionic salts with tropylium, while the acids with $K_a \leq 6.8 - 1.75 \cdot 10^{-5}$ should give covalent compounds with tropylium.

This conclusion is supported by the results obtained when tropylium bromide or tropylium perchlorate is reacted with cyclopentadienyllithium. Here it is not the ionic salt of tropylium with the cyclopentadienyl anion that is formed ($C_7H_7^+C_6H_5^-$), but instead it is the covalent cyclopentadienyl-tropylium (cyclopentadienylcycloheptatriene)* according to the scheme

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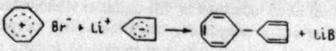
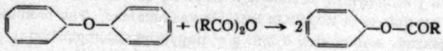
* Here and below we put to one side the question of whether the covalent derivatives of tropylium have a cycloheptatriene or a norcaradiene structure (cf. [4]).



The formation of a covalent compound is explained by the weakly acidic properties of cyclopentadiene, and consequently by the substantial nucleophilicity of the $C_5H_5^-$ anion.

Tropylium acetate and the benzoate were synthesized by the acylation of tropylium oxide (dicycloheptatrienyl ether) with respectively acetic and benzoic anhydrides according to the scheme



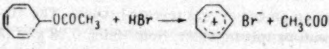
The preparation of cycloheptatrienylium esters by the acylation of tropylium oxide with the corresponding anhydrides can apparently have quite general significance.

Attempts to obtain tropylium acetate by the exchange reaction of tropylium perchlorate with potassium acetate in either water or alcohol proved unsuccessful. In water medium, instead of tropylium acetate, we isolated tropylium oxide. We were also unable to obtain tropylium benzoate either by the exchange reaction of potassium benzoate with tropylium perchlorate in water, or by the exchange decomposition of silver benzoate and tropylium bromide in either alcohol or nitromethane. Instead of tropylium benzoate, we isolated benzoic acid and tropylium oxide. These results are explained by the instability of the cycloheptatrienylium esters and their great tendency to hydrolyze.

Actually, the ester linkage in both the tropylium acetate and benzoate proved to be extremely unstable. Thus, tropylium acetate is readily hydrolyzed by water with the formation of tropylium oxide

$$2C_7H_7{-}OCOCH_3 + H_2O \rightarrow (C_7H_7)_2O + 2CH_3COOH$$

The acetate is instantaneously decomposed by hydrochloric acid with the formation of the tropylium salt. The ester linkage is also easily cleaved when tropylium acetate is treated with dry hydrogen bromide.

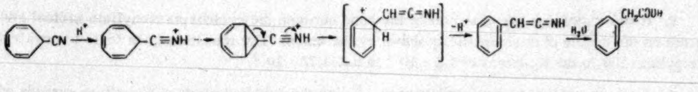


The alkaline hydrolysis of tropylium acetate also proceeds with great ease – the compound can be titrated in the cold with alkali solution.

$$2C_7H_7{-}OCOCH_3 + 2NaOH \rightarrow (C_7H_7)_2O + 2CH_3COONa$$

The covalent bond $C_7H_7{-}X$ in tropylium cyanide and in cyclopentadienyl-tropylium proved to be much more stable. When treated with either hydrogen bromide or with concentrated hydrochloric acid, tropylium cyanide is not converted to the tropylium salt.

It is interesting that in the acid hydrolysis of tropylium cyanide partial isomerization occurs, and phenylacetic acid is formed. Apparently, the isomerization of tropylium cyanide is linked with the formation of the nitrilium salt in acid medium, and the probable mechanism for its formation (by analogy with the mechanisms for the rearrangements of tropolones and tropones [5]) can be depicted by the scheme



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* The covalent character of cyclopentadienylheptatriene is also indicated by Doering [6].

EXPERIMENTAL

Tropylium Acetate. To 1.9 g of tropylium perchlorate [3] was added 10 ml of saturated sodium bicarbonate solution. The aqueous solution was extracted with ether, the ether extracts were dried over Na_2SO_4, and the ether was vacuum-distilled. The tropylium oxide obtained in this manner, without further purification, was heated for 1 hour on the water bath with 6 ml of acetic anhydride. Then the acetic anhydride was vacuum-distilled, and the residue was fractionally distilled. We obtained 0.55 g of tropylium acetate (yield 37%, based on tropylium perchlorate); b.p. 52-55° (1 mm), $n^{19}D$ 1.5397, d^{20}_4 1.083.

Found %: C 72.28, 72.18; H 6.49, 6.49; $C_9H_{10}O_2$. Calculated %: C 71.98; H 6.71.

Tropylium acetate is readily soluble in ether, benzene, petroleum ether and carbon tetrachloride. It rapidly darkens in the air.

A solution of 0.0573 g of tropylium acetate in 3 ml of dry carbon tetrachloride was saturated with dry hydrogen bromide. Here a yellow precipitate of tropylium bromide was obtained. The bromide was dissolved in alcohol and then treated with chloroplatinic acid to give 0.0661 g of tropylium chloroplatinate; yield 60%.

0.3432 g of tropylium acetate was dissolved in 3 ml of concentrated hydrochloric acid. The addition of chloroplatinic acid gave 0.4576 g of tropylium chloroplatinate; yield 68%.

A solution of 0.0941 g of tropylium acetate in alcohol was titrated with 0.1 N alcoholic NaOH solution using phenolphthalein as indicator. The amount of alkali consumed for the titration was 5.1 ml (81% of the theoretical).

Tropylium Benzoate. To the tropylium oxide obtained from 4.75 g of tropylium perchlorate was added a solution of 1.5 g of benzoic anhydride in absolute ether. The mixture was boiled for 30 minutes, the ether was distilled off, anhydrous benzene was added to the residue, and the boiling was continued for another 1.5 hours. Vacuum-distillation gave 0.31 g of tropylium benzoate with b.p. 76-82° (2 mm); yield 11% (calculated on the benzoic anhydride).

Found %: C 79.56, 79.44; H 5.92, 5.82. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

Tropylium benzoate is readily soluble in nonpolar solvents; it darkens rapidly in the air.

Hydrolysis of Tropylium Cyanide. A mixture of 0.9 g of tropylium cyanide [obtained from the reaction of 1.9 g of tropylium perchlorate with 1 g of KCN in 25 ml of water; b.p. 51-53° (1.5 mm), $n^{20}D$ 1.5310, d^{20}_4 1.017] and 4 ml of concentrated hydrochloric acid was refluxed for 2 hours. The solution was extracted with ether. The ether extracts were extracted with 10% NaOH solution, which was then acidified with hydrochloric acid and again extracted with ether. This purification procedure was repeated twice. The ether extracts were dried and evaporated. The residue was extracted with petroleum ether, from which 0.08 g of phenylacetic acid with m.p. 76° was isolated; the latter does not depress the melting point with the authentic specimen.

Cyclopentadienylcycloheptatriene. To 0.4 g of freshly distilled cyclopentadiene was added a solution of butyllithium (from 0.9 g of $n\text{-}C_4H_9Br$ and 0.15 g of Li). To the obtained suspension of cyclopentadienyllithium was added 0.75 g of finely pulverized tropylium bromide, and the mixture was stirred for 1 hour. Then the ether was distilled off, and the residue was extracted with petroleum ether. Removal of the petroleum ether by distillation, followed by vacuum-distillation, gave cyclopentadienylcycloheptatriene with b.p. 82-84° (4 mm); yield 0.44 g (56%, based on tropylium bromide); $n^{20}D$ 1.5610. The compound is readily soluble in ether, benzene and petroleum ether, and insoluble in water; it does not give a precipitate of tropylium chloroplatinate when treated with H_2PtCl_6.

SUMMARY

1. Tropylium acetate, tropylium benzoate and cyclopentadienylcycloheptatriene were synthesized, proving to be covalent compounds.

2. It was shown that the character of the bond between the cycloheptatrienylium radical and the anion depends on the degree of nucleophilicity shown by the anion. The transition from ionic to covalent derivatives of tropylium lies in the K_a limits of $1.2 \cdot 10^{-4}$ to $6.3\text{-}1.75 \cdot 10^{-5}$.

3. It was shown that rearrangement occurs during the acid hydrolysis of tropylium cyanide with the formation of phenylacetic acid.

Received April 15, 1957

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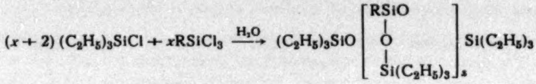
SIMULTANEOUS HYDROLYSIS OF MONO- AND TRIFUNCTIONAL ALKYL(ARYL)CHLOROSILANES

K. A. Andrianov, M. Ia. Levshuk, S. A. Golubtsov and T. A. Krasovskaia

The synthesis of most polymeric organosilicon compounds of the polyorganosiloxane type is accomplished by the method of simultaneous hydrolysis of two, and at times of a greater number of monomeric organosilicon compounds, represented by the alkyl- or arylchlorosilanes, or by the substituted esters of orthosilicic acid. There is very little information in the literature regarding the simultaneous hydrolysis of the indicated monomers. It is usually assumed that when a mixture of two alkyl- or arylchlorosilanes is hydrolyzed it is the polymeric product of the simultaneous hydrolysis of these two compounds that is formed. In studying this process for mixtures of compounds with different functionality, we found that this reaction goes in part toward the formation of not the simultaneous hydrolysis product, but instead to a mixture of the two polymers. Thus, for example, when we attempted to prepare polymers with a branched-chain structure from an aryltrichlorosilane and triethylchlorosilane by scheme (1) we found that if the reaction was run at a temperature not exceeding 20° the hydrolysis product was a mixture of hexaethyldisiloxane and tarry phenylsiloxane polymer, formed according to schemes (2) and (3).



$$(x+2)\,(C_2H_5)_3SiCl + xRSiCl_3 \xrightarrow{H_2O} (C_2H_5)_3SiO\left[\begin{array}{c} RSiO \\ | \\ O \\ | \\ Si(C_2H_5)_3 \end{array}\right]_x Si(C_2H_5)_3 \qquad (1)$$

where $R = C_6H_5$ or C_6H_4Cl.

$$2(C_2H_5)_3SiCl \xrightarrow{H_2O} (C_2H_5)_3SiOSi(C_2H_5)_3 \qquad (2)$$

$$xRSiCl_3 \xrightarrow{H_2O} (RSiO_{1.5})_x \qquad (3)$$

As our experiments revealed, neither changing the molar ratios nor the acidity of the medium, nor using various solvents during hydrolysis, made it possible to suppress reactions (2 and (3), and direct the process toward

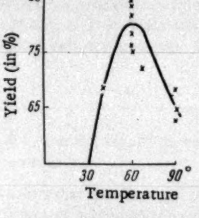


Fig. 1. Simultaneous hydrolysis of phenyltrichlorosilane and triethylchlorosilane.

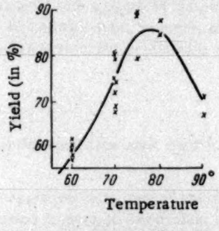


Fig. 2. Simultaneous hydrolysis of chlorophenyltrichlorosilane and triethylchlorosilane.

the formation of the simultaneous hydrolysis product according to reaction (1). Quite probably this is due to the existence of considerable differences in the hydrolysis and condensation rates of compounds with different functionality.

TABLE 1

Simultaneous Hydrolysis of Phenyltrichlorosilane and Triethylchlorosilane

Change (in g)		g-moles triethylchlorosilane per g-mole phenyltrichlorosilane	Temperature	Yield of hydrolysis product (in g)	Yield (in %)	
phenyltrichlorosilane	triethylchlorosilane				cohydrolysis product	still residue
18.7	40	3.0	4°	39	Absent	23.8*
18.7	40	3.0	20	41	Absent	24.7*
18.7	80	6.0	20	71	Absent	25.3*
18.7	40	3.0	40	42	68	12.6
18.7	40	3.0	60	42	78	9.4
148	348	3.3	60	351	76	20.0
148	348	3.3	60	359	81	12.0
106	340	4.5	60	396	75	16.0
211	677	4.5	60	666	84	11.0
106	451	6.0	60	410	86	Traces
211	903	6.0	60	805	83	7.2
106	248	3.3	70	314	73	8.0
18.7	40	3.0	90	39	65	9.0
106	452	6.0	90	412	63	12.0
106	226	3.0	90	262	67	17.0

TABLE 2

Simultaneous Hydrolysis of Chlorophenyltrichlorosilane and Triethylchlorosilane

Change (in g)		g-moles triethylchlorosilane per g-mole phenyltrichlorosilane	temp.	Yield of hydrolysis product (in g)	Yield (in %)	
chlorophenyltrichlorosilane	triethylchlorosilane				cohydrolysis product	still residue
24.6	67.7	4.5	60°	66	70	71
24.6	67.7	4.5	60	76	61	26
54.1	109	3.3	60	102	61	12
73.8	148	3.3	60	150	62	27
73.8	148	3.3	60	149	60.5	19
123.5	226	3.0	60	343	58.6	23
123	226	3.0	60	266	50	33
173	348	3.3	60	398	63	30
173	348	3.3	60	—	60	29
369	745	3.3	70	969	69	21
73.8	149	3.3	70	165	76	11
73.8	203	4.5	70	219	80	18
73.8	203	4.5	70	231	73	9
73.8	149	3.3	70	191	81	17
73.8	203	4.5	70	192	68	6
73.8	149	3.3	70	168	75	9
73.8	149	3.3	75	170	89	7
213	430	3.3	75	540	80	8
246	677	4.5	75	709	90	7
73.8	149	3.3	80	187	88	11
73.8	149	3.3	80	173	86	11
246	677	4.5	80	704	85	6
73.8	149	3.3	90	—	72	14
73.8	149	3.3	90	149	68	12

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* Hard tar.

It was natural to assume that the temperature coefficients of the rates of the indicated reactions are different; for this reason we attempted to accomplish the simultaneous hydrolysis of compounds with different functionality by varying the reaction temperature. Experiment revealed that the assumption made is valid, and that running the hydrolysis at elevated temperature favors obtaining simultaneous hydrolysis products, and not a mechanical mixture of the two polymers.

The relationship between the yield of simultaneous hydrolysis product and the reaction temperature for the case of the hydrolysis of a mixture of phenyltrichlorosilane and triethylchlorosilane is shown in Fig. 1. The optimum temperature for running the process according to scheme (1) is 60°. A similar relationship between the yield of cohydrolysis product and the temperature for a mixture of chlorophenyltrichlorosilane and triethylchlorosilane is shown in Fig. 2 (in this case the optimum temperature for simultaneous hydrolysis is 90°).

EXPERIMENTAL

Water was placed in a round-bottomed flask, fitted with dropping funnel, thermometer, stirrer and reflux condenser, and its temperature was brought up to the reaction temperature by heating the flask on the water bath. A mixture of triethylchlorosilane and phenyltrichlorosilane (molar ratio 3 : 1) was then added to the flask with stirring and at a constant temperature. The hydrolysis product was separated from the hydrochloric acid, washed, dried, and heated at 200° for 1 hour, after which it was fractionally distilled at a pressure of 2 mm. The 80-110° fraction proved to be hexaethyldisiloxane; the 110-250° fraction was the liquid product of simultaneous hydrolysis. The residue was a liquid high-molecular product of incomplete cohydrolysis, or if the reaction was run at low temperature it represented solid phenylsiloxane polymer. The yield of simultaneous hydrolysis products was calculated in percent of the theoretical according to reaction (1), after substracting the hexaethyldisiloxane. The results of the experiments on the simultaneous hydrolysis of mixtures of phenyltrichlorosilane and triethylchlorosilane at various temperatures are shown in Table 1, while the results of the experiments on the hydrolysis of mixtures of chlorophenyltrichlorosilane and triethylchlorosilane, run by a similar procedure, are shown in Table 2.

SUMMARY

It was established that when the hydrolysis of mixtures of mono- and trifunctional alkyl(aryl)chlorosilanes (phenyl- or chlorophenyltrichlorosilane with triethylchlorosilane) is run at room temperature the reaction product is a mixture of the two polymers (hexaethyldisiloxane and polyphenylsiloxane resin). The product of the simultaneous hydrolysis of phenyl- or chlorophenyltrichlorosilane with triethylchlorosilane is formed if the reaction is run at elevated temperature.

Received January 19, 1957

SYNTHESIS AND PROPERTIES OF TETRAKIS(TRIBENZYLSILOXY)SILANE AND TETRAKIS(TRIBENZYLSILOXY)METHANE

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Tetrakis(triarylsiloxy)silanes of type $[Ar_3SiO]_4Si$ and their corresponding analogs – the tetrakis(triarylsiloxy)-methanes – have not been reported up to now. In one of our studies [1] it was established that the reaction of excess sodium triphenylsilanolate with either silicon tetrachloride or tetrafluoride, due to the high steric hindrance shown by the triphenylsiloxy group, yields only the corresponding tris(triphenylsiloxy)halosilane of type $[Ar_3SiO]_3SiX$.

In the present study a substitution of the less sterically hindered benzyl radicals for the phenyl radicals enabled us to successfully accomplish the synthesis of tetrakis(tribenzylsiloxy)silane according to the equation

$$4(C_6H_5CH_2)_3SiONa + SiCl_4 \rightarrow [(C_6H_5CH_2)_3SiO]_4Si + 4NaCl$$

This compound was obtained as colorless crystals with m.p. 204-205°, and stable to both dilute acids and alkalies.

Under similar conditions, starting with sodium tribenzylsilanolate and carbon tetrabromide, we obtained tetrakis(tribenzylsiloxy)methane with m.p. 217-218° in 42% yield.

Using a spectrometer with NaCl prism we investigated[*] the infrared absorption spectra of tetrakis(tribenzylsiloxy)silane and tetrakis(tribenzylsiloxy)methane, pelleted with potassium bromide powder, in the 6-15 μ region.

The frequencies (in cm^{-1}) of the absorption bands and the conjectural interpretation of some of them are given below.

Next, starting with sodium triphenylsilanolate and carbon tetrabromide, we obtained tris(triphenylsiloxy)bromomethane with m.p. 231-232°. The tris(triphenylsiloxy)methane obtained by us earlier [2] had m.p. 222-223°.

It was shown that the Si–O–Si bond in tris(triphenylsiloxy)halosilanes is more resistant to the action of alkali solution than is the Si–O–C bond in the similarly constructed tris(triphenylsiloxy)bromomethane. Thus, when tris(triphenylsiloxy)bromomethane is treated with alkali the Si–O–C bond suffers rupture with the formation of triphenylsilanol according to the equation

$$[(C_6H_5)_3SiO]_3CBr \xrightarrow[HOH]{NaOH} 3(C_6H_5)_3SiOH$$

At the same time, the Si–O–Si bond in either tris(triphenylsiloxy)chlorosilane or tris(triphenylsiloxy)fluorosilane remains unchanged under the above indicated conditions, and only as the result of halogen hydrolysis is the corresponding tris(triphenylsiloxy)silanol formed [1].

EXPERIMENTAL

The tribenzylsilanol used as starting product was obtained by the saponification of tribenzylfluorosilane, obtained [3] by the reaction of benzylmagnesium chloride with silicon tetrafluoride, in alcohol-ether mixture with 2 N caustic solution.

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[*] The author wishes to thank A. N. Lazarev for taking the infrared absorption spectra.

$[(C_6H_5CH_2)_3SiO]_4Si$	$[(C_6H_5CH_2)_3SiO]_4C$	Interpretation
1610 (m)	1620 (v w)	Valence vibrations of the C_6H_5 ring
1470 (s)	1470 (w)	
1447 (s)	1427 (s)	Deformations of the CH_2 group
1397 (m)	1385 (w)	
1208 (s)	1191 (m)	Vibrations of the $-\overset{\overset{C}{\vert}}{\underset{\underset{C}{\vert}}{Si}}-C$ group
1161 (s)	1151 (m)	Vibrations of the C_6H_5 group
—	1117 (v w)	Valence vibrations of C–O
1092 (vs)	1092 (vw)	Valence vibrations of Si–O
1056 (m)	1070—1050 (m)	Vibrations of the C_6H_5 group and the C–C bond
1027 (m)	1027 (m)	
997 (m)	995 (m)	
968 (m)		
907 (s)	918 (vw)	
848 (m)	856 (w)	
822 (s)	—	
810 (s)	—	
780 (vs)	—	
763 (s)	—	
746 (m)	743 (m)	Nonplanar CH deformations of the C_6H_5 group
737 (m)	736 (s)	
—	708 (vs)	
693 (s)	694 (s)	Nonplanar CH deformations of the C_6H_5 group

Legend. **1. The intensity characteristics of the bands are given in parentheses;** vs — very strong, s — strong, m — medium, w — weak, vw — very weak.
2. Some of the bands in the 690-750 cm^{-1} region may be due to Si–C vibrations.
3. Some weak bands were observed in the 1325-1240 cm^{-1} region, caused by trace impurities in the KBr.

Tetrakis(tribenzylsiloxy)silane. In a flask, fitted with reflux condenser, was placed 32 g of tribenzylsilanol, dissolved in 300 ml of dry benzene, and 3 g of sodium metal; the flask contents were heated under reflux for 2 hours, and after the sodium tribenzylsilanolate had formed the solution was cooled to 5-7°, a solution of 4.2 g of silicon tetrachloride in 50 ml of benzene added, and the mixture heated an additional 4 hours under reflux. After separating the formed sodium chloride the isolated crystals were recrystallized twice from benzene. We obtained 24.2 g of coarse transparent crystals (yield 75.4%, based on silicon tetrachloride); m.p. 204-205°.

Found %: Si 10.2, 10.5. $C_{84}H_{84}O_4Si_5$. Calculated %: Si 10.8.

Tetrakis(tribenzylsiloxy)methane. Sodium tribenzylsilanolate was prepared from 16 g of tribenzylsilanol, 200 ml of benzene and 2 g of sodium. To the solution, cooled to 0°, was added 4 g of carbon tetrabromide, dissolved in 100 ml of benzene; the mixture was heated under reflux for 8 hours. After separating the sodium bromide the isolated crystals were recrystallized from benzene. Transparent crystals. Yield 6.5 g (42%, based on carbon tetrabromide); m.p. 217-218°.

Found %: C 80.2, 80.3; Si 8.5, 8.5; H 6.9, 7.0. $C_{85}H_{84}O_4Si_4$. Calculated %: C 79.7; Si 8.8; H 6.6.

Tris(triphenylsiloxy)bromomethane. Sodium triphenylsilanolate was prepared from 27.6 g of triphenylsilanol in 300 ml of benzene and 3 g of sodium. To the solution, cooled to 0°, was added 4 g of carbon tetrabromide in 50 ml of benzene; the mixture was heated under reflux for 8 hours. After separating the sodium bromide the isolated crystals were recrystallized from benzene. Yield 4.7 g (30.2%, based on carbon tetrabromide). Fine crystals; m.p. 231-232°.

Found %: Si 8.0, 7.8; Br 7.1, 7.3. $C_{64}H_{63}O_3BrSi_3$. Calculated %: Si 8.1, Br 7.6.

Reaction of Tris(triphenylsiloxy)bromomethane With Alkali. In a flask, fitted with reflux condenser, was placed 1.84 g of tris(triphenylsiloxy)bromomethane in 50 ml of dioxan and 5 ml of 2 N NaOH; the mixture was heated under reflux on the water bath for 2 hours. Then the solution was treated with 50 ml of water and the obtained flocculent precipitate was filtered and recrystallized from ether. We obtained 1.32 g of triphenylsilanol, identified by its melting point.

SUMMARY

1. The previously unknown tetrakis(tribenzylsiloxy)silane and tetrakis(tribenzylsiloxy)methane were synthesized and their infrared absorption spectra investigated.

2. It was shown that the Si—O—C bond in tris(triphenylsiloxy)bromomethane is less stable to the action of alkali solution than is the Si—O—Si bond in tris(triphenylsiloxy)halosilanes.

Received January 22, 1957

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*Original Russian pagination. See C. B. Translation.

TRIMETHOXY- AND TRIARYLOXYPHOSPHAZOSULFONITROPHENYLS AND DIESTERS OF NITROPHENYLSULFONAMIDOPHOSPHORIC ACIDS

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The trimethoxy- and triaryloxyphosphazosulfonitrophenyls (I) and the diesters of nitrophenylsulfonamidophosphoric acids (II) were synthesized for the purpose of studying their insecticidal properties and as starting substances for the preparation of N-phosphoric acid derivatives of sulfanilamides.

Compounds of type (I) were obtained by the reaction of trichlorophosphazosulfonitrophenyls [1] with either sodium methylate or arylate in benzene solution [2] according to the scheme

$$NO_2C_6H_4SO_2N{=}PCl_3 + 3NaOR \rightarrow 3NaCl + NO_2C_6H_4SO_2N{=}P(OR)_3$$

In this manner we obtained the trimethoxy-, triphenoxy-, tris(p-chlorophenoxy)-, tris(o-nitrophenoxy)- and tris(p-nitrophenoxy)-phosphazosulfo-o-, m- and p-nitrophenyls (I) (Table 1).

Compounds of type (I) are colorless crystalline compounds of a neutral character, insoluble in water. The trimethoxyphosphazosulfonitrophenyls (III) when boiled with 96% alcohol for 1 hour are saponified to the corresponding diesters (XIV). The triphenoxyphosphazosulfonitrophenyls (IV) do not change under these conditions. The trimethoxy- and triphenoxyphosphazosulfonitrophenyls have comparatively low melting points (in the range 56-104°). Compounds of type (I) are not saponified when treated with aqueous alkali solutions, which is explained by their insolubility in water. In aqueous-alcohol alkali solutions they are easily saponified to (II). However, compounds of the (II) type are obtained more conveniently from the dichlorides of nitrophenylsulfonamidophosphoric acids [1] by reaction with sodium methylate or arylates in dioxan solution by the scheme

$$NO_2C_6H_4SO_2NHPOCl_2 + 3NaOR \rightarrow 3NaCl + ROH +$$
$$+ [NO_2C_6H_4SO_2NPO(OR)_2]^-Na^+ \xrightarrow{+H^+} NO_2C_6H_4SO_2NHPO(OR)_2$$

In this manner we obtained the dimethyl, diphenyl, di-(p-chlorophenyl), di-(o-nitrophenyl) and di-(p-nitrophenyl) esters of the o-, m- and p-nitrophenylsulfonamidophosphoric acids (II) (Table 2). It is possible to isolate the (II) compounds as the salts, but it is more convenient to isolate them as the free diesters. The (II) compounds are comparatively high-melting (in the range 134-194°), colorless, crystalline substances, insoluble in water, and melting considerably higher than the corresponding (I) compounds, with the exception of the two p-nitrophenol esters (XI and XIII), which melt below the corresponding (I) compounds. The (II) compounds are monobasic acids, capable of being titrated accurately in the presence of phenolphthalein, and giving sodium salts that crystallize well and are readily soluble in water. It is interesting to mention that the sodium salts of the p-chlorophenyl esters of nitrophenylsulfonamidophosphoric acids, when their aqueous solutions are extracted with ether, pass almost entirely into the ether layer. The sodium salts of the other diesters are not extracted from their aqueous solutions by ether.

EXPERIMENTAL

Trimethoxyphosphazosulfonitrophenyls (III). To a solution of 0.06 g-mole of sodium methylate in 30 ml of methanol, cooled to 0°, was slowly added with mechanical stirring a solution of 0.02 g-mole of trichlorophosphazosulfonitrophenyl in 40 ml of benzene at such a rate that the temperature was maintained in the range 0 to +5°. After all of the solution of phosphazo compound had been added, the reaction mixture was heated at 50° for 30 minutes. The solvents were removed by distillation in vacuo, the residue was treated with 40 ml of water, and

TABLE 1

Trimethoxy- and Triaryloxyphosphazosulfonitroaryls (I) of Type $ArC_6H_4SO_2N{=}P(OR)_3$

Number of compound		Ar	R	Yield (in %)	Crystalline form, solvent	Melting point	Formula	(in %)	
								found	calculated
III	—	o-$NO_2C_6H_4$	CH_3	80.0	Needles from CCl_4	68—70°	$C_9H_{13}O_7N_2SP$	8.67	8.64
	—	m-$NO_2C_6H_4$	CH_3	81.3	Needles from CCl_4	57—59		8.72	8.64
	—	p-$NO_2C_6H_4$	CH_3	88.7	Needles from CCl_4	94—96		8.78	8.64
IV	—	o-$NO_2C_6H_4$	C_6H_5	84.2	Prisms from alcohol	78—79	$C_{24}H_{19}O_7N_2SP$	5.62	5.49
	—	m-$NO_2C_6H_4$	C_6H_5	81.0		56—58		5.47	5.49
	VIII	p-$NO_2C_6H_4$	C_6H_5	80.0	Prisms from alcohol	101—104		5.66	5.49
V	IX	o-$NO_2C_6H_4$	p-ClC_6H_4	70.0	Needles from CCl_4	139—141	$C_{24}H_{16}O_7N_2Cl_3SP$	4.58	4.56
	X	m-$NO_2C_6H_4$	p-ClC_6H_4	75.0	Prisms from alcohol	133—135		4.64	4.56
	—	p-$NO_2C_6H_4$	p-ClC_6H_4	64.2	Needles from CCl_4	151—153		4.56	4.56
VI	—	o-$NO_2C_6H_4$	o-$NO_2C_6H_4$	90.0	Prisms from benzene	140—141	$C_{24}H_{16}O_{13}N_5SP$	10.83	10.83
	—	m-$NO_2C_6H_4$	o-$NO_2C_6H_4$	82.0	Prisms from benzene	135—137		10.91	10.83
	—	p-$NO_2C_6H_4$	o-$NO_2C_6H_4$	95.0	Prisms from benzene	159—161		10.76	10.83
VII	XI	o-$NO_2C_6H_4$	p-$NO_2C_6H_4$	79.0	Needles from dioxan	199—202		10.91	10.83
	XII	m-$NO_2C_6H_4$	p-$NO_2C_6H_4$	83.0	Prisms from benzene	175—177		10.73	10.83
	XIII	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$	85.0	Prisms from acetone	202—203		10.82	10.83

the obtained crystalline precipitate was suction-filtered, washed with water, and air-dried. The trimethoxyphosphazosulfo-m-nitrophenyl deposited as an oil, which was extracted with benzene. Removal of the benzene by distillation left a viscous oil, which soon crystallized completely.

Triphenoxyphosphazosulfonitrophenyls (IV) and Tris(p-chlorophenoxy)phosphazosulfonitrophenyls (V). To 0.045 g-mole of well-dried and pulverized sodium phenate or sodium p-chlorophenate was added in one portion a solution of 0.015 g-mole of trichlorophosphazosulfonitrophenyl in 30 ml of dry benzene and the mixture was stirred vigorously. When stormy reaction had ended, the mixture was heated under reflux on the water bath for 1 hour. The benzene was distilled in vacuo and the residue was treated with 25 ml of 1 N aqueous sodium hydroxide solution. Here (V) and (VIII) deposited immediately as crystalline precipitates. The triphenoxyphosphazosulfo-o-nitrophenyl deposited as an oil, which crystallized completely when rubbed with a glass rod. The triphenoxyphosphazosulfo-m-nitrophenyl was synthesized by a similar procedure, but in dioxan solution.

Tris(o-nitrophenoxy)- (VI) and Tris(p-nitrophenoxy)-phosphazosulfonitrophenyls (VII). The reaction was run in the same manner as for (IV) and (V), but here it is necessary to heat the reaction mixture under reflux and with stirring for not less than 5 hours. After removal of the benzene by distillation in vacuo the residue was treated with 25 ml of 1 N caustic solution, the crystalline precipitate suction-filtered, and then washed 3 times each with water, alcohol and ether to remove free nitrophenol. The (VI) and (VII) compounds obtained in this manner are practically pure and melt within three degrees. All the (I) compounds are insoluble in water, ether and petroleum ether, and readily soluble at room temperature in acetone and dioxan, with the exception of (VIII) and (XI), which dissolve in dioxan only on heating. (III) and (IV) are readily soluble in ethyl acetate, and can be recrystallized from either alcohol or benzene. The (VI) compounds are insoluble in alcohol, and can be recrystallized from benzene. (VI) and (VII) are insoluble in carbon tetrachloride, (III) and (IX) are slightly soluble, and (IV), (VIII) and (X) are somewhat soluble in this solvent.

TABLE 2

Dimethyl and Diaryl Esters of Nitrophenylsulfonamidophosphoric Acids (II) of Type $ArSO_2NHPO(OR)_2$

Number of compound		Ar	R	Yield (in %)	Recrystallization solvent	Melting point	Formula	N (in %) found	N (in %) calculated	No. of equivalents found	No. of equivalents calculated
XIV	XIX	$o\text{-}NO_2C_6H_4$	CH_3	80.0	benzene	134—136°	$C_8H_{11}O_7N_2SP$	9.18	9.03	1.004	1.000
	—	$m\text{-}NO_2C_6H_4$	CH_3	87.0	alcohol	145—148		9.17	9.03	1.008	1.000
	XX	$p\text{-}NO_2C_6H_4$	CH_3	82.3	alcohol	175—177		8.98	9.03	1.008	1.000
XV	—	$o\text{-}NO_2C_6H_4$	C_6H_5	84.5	benzene	156—158	$C_{18}H_{15}O_7N_2SP$	6.55	6.45	1.003	1.000
	—	$m\text{-}NO_2C_6H_4$	C_6H_5	83.7	benzene	146—147		6.58	6.45	0.990	1.000
	—	$p\text{-}NO_2C_6H_4$	C_6H_5	88.2	benzene	192—193		6.45	6.45	1.010	1.000
XVI	XXI	$o\text{-}NO_2C_6H_4$	$p\text{-}ClC_6H_4$	70.0	benzene	149—151	$C_{18}H_{13}O_7N_2Cl_2SP$	5.60	5.56	1.020	1.000
	—	$m\text{-}NO_2C_6H_4$	$p\text{-}ClC_6H_4$	70.5	benzene	153—155		5.71	5.56	1.008	1.000
	—	$p\text{-}NO_2C_6H_4$	$p\text{-}ClC_6H_4$	80.0	benzene	163—165		5.63	5.56	1.005	1.000
XVII	—	$o\text{-}NO_2C_6H_4$	$o\text{-}NO_2C_6H_4$	71.0	alcohol	171—174	$C_{18}H_{13}O_{11}N_4SP$	10.64	10.69	1.000	1.000
	—	$m\text{-}NO_2C_6H_4$	$o\text{-}NO_2C_6H_4$	72.5	alcohol	175—178		10.76	10.69	1.006	1.000
	—	$p\text{-}NO_2C_6H_4$	$o\text{-}NO_2C_6H_4$	71.6	water	167—170		10.69	10.69	1.010	1.000
XVIII	—	$o\text{-}NO_2C_6H_4$	$p\text{-}NO_2C_6H_4$	74.2	alcohol	188—191		10.71	10.69	1.014	1.000
	—	$m\text{-}NO_2C_6H_4$	$p\text{-}NO_2C_6H_4$	87.8	alcohol	191—194		10.78	10.69	1.005	1.000
	XXII	$p\text{-}NO_2C_6H_4$	$p\text{-}NO_2C_6H_4$	89.2	Na salt was reprecipitated	165—168		10.77	10.69	1.020	1.000

(VII), (VIII), and (X) are difficultly soluble in alcohol, and (IX) is somewhat more soluble. (X), (XI) and (XIII) are difficultly soluble in benzene, and (VII), (IX) and (XII) are much more soluble in this solvent. Thus, the solubility of (III), (IV) and (VI) is determined mainly by the nature of the ester groups (OR) and changes but slightly when the position of the nitro group in the nitroarylsulfonyl grouping ($NO_2C_6H_4SO_2$) is changed. In the case of the p-chlorophenol (V) and p-nitrophenol (VII) derivatives the position of the nitro group in $NO_2C_6H_4SO_2$ exerts a very great influence on the solubility. The p-nitrophenol derivatives (VII) are the most difficultly soluble in the common organic solvents.

Dimethyl Esters of Nitrophenylsulfonamidophosphoric Acids (XIV). To a solution of 0.06 g-mole of sodium methylate in 35 ml of methanol, with ice-water cooling and vigorous stirring, was added 0.02 g-mole of finely pulverized nitrophenylsulfonamidophosphoryl dichloride. On conclusion of quite violent reaction the mixture was boiled for 10 minutes under reflux, the benzene was vacuum-distilled, and the residue, a mixture of sodium salt (XIV) and sodium chloride, was treated with 20 ml of 2 N hydrochloric acid. Here (XIV) deposited as an oil, which crystallized completely when cooled and rubbed with a glass rod. The product was suction-filtered, washed with cold water, and air-dried.

Diphenyl (XV), Di(p-chlorophenyl) (XVI), Di(o-nitrophenyl) (XVII) and Di(p-nitrophenyl) (XVIII) Esters of Nitrophenylsulfonamidophosphoric Acids. To 0.06 g-mole of well-dried and pulverized sodium arylate was added with stirring a solution of 0.02 g of nitrophenylsulfonamidophosphoryl dichloride in 40 ml of dioxan, and this was accompanied by considerable heat evolution. The mixture was boiled under reflux with stirring for 1 hour in the case of (XV), for 3 hours in the case of (XVI), and for 6 hours in the case of (XVII) and (XVIII). Then the solvent was removed by distillation in vacuo, the residue, representing a mixture of diester sodium salts, sodium chloride and the phenol, was dissolved in water, and the obtained solution extracted with ether (3 times with 15-ml portions) to remove the phenol formed in the reaction. The water layer was filtered and then acidified with hydrochloric acid until acid to Congo, and here the free diesters deposited either as needlelike crystals or as an oil, which soon crystallized completely. In the case of (XVI) the ether extracted almost all of the diester sodium salt from the water solution, and for this reason the dry residue obtained after evaporation of the ether was treated with 20 ml of 2 N hydrochloric acid, then with 30 ml ether, and the whole shaken vigorously. Three layers were formed when this was done – an aqueous layer, an ether layer, and an oil layer containing the free (XVI) compounds, which on shaking soon crystallized as coarse needles. The product was suction-filtered, washed with water and ether, and then air-dried.

All the (II) compounds are readily soluble in acetone at 20°, readily soluble in boiling alcohol, and insoluble in cold water, ether, carbon tetrachloride and petroleum ether. (XVII), (XVIII), (XIX) and (XX) are readily soluble in hot water, while the (XVI) compounds are only slightly soluble. The (XVI) compounds are readily soluble in boiling benzene, while (XVII) and (XVIII) are insoluble in benzene. All the (II) compounds crystallize as needles. All the (II) compounds give well crystallizing salts when treated with 1 equivalent of caustic solution. Thus, for example, (XXII) gives the sodium salt of the di(p-nitrophenyl) ester of p-nitrophenylsulfonamidophosphoric acid (XXIII), readily soluble in water, and crystallizing from alcohol as coarse needles (m.p. 220-222°).

Found %: N 10.21. $C_{18}H_{12}O_{11}N_4SPNa$. Calculated %: N 10.26.

The treatment of (XXIII) with mineral acids yields (XXII).

SUMMARY

The trimethoxy- and triaryloxyphosphazosulfonitrophenyls and the dimethyl and diaryl esters of nitrophenylsulfonamidophosphoric acids were obtained and described.

Received December 24, 1956

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*Original Russian pagination. See C. B. Translation.

SUBSTITUTED IMIDO- AND MONOARYLSULFAMIDES

A. V. Kirsanov and Iu. M. Zolotov

Earlier imidosulfamide was a practically unavailable substance [1], while the substituted imidosulfamides were not known. At the present time imidosulfamide is quite readily available [2], and the 3-methyl- and 3-ethylimidosulfamides have been obtained from it [3]. The 1- and 1,5-substituted imidosulfamides have been unknown up to now.

The free imidosulfamide in its chemical properties is a monobasic acid, in strength almost equal to that of either sulfuric or hydrochloric acid [2]. For this reason the 3-substituted derivatives of imidosulfamide [3] should be called esters of imidosulfamide, which is in accord with their chemical properties, and only the 1- and 1,5-substituted imidosulfamides should be regarded as being substituted imidosulfamides.

A second method for the preparation of imidosulfamide [2] proved suitable for the preparation of the 1,5-disubstituted and 1,1,5,5-tetrasubstituted imidosulfamides, and consequently this method is a general method for the preparation of not only the unsubstituted, but also the 1,5-di- and 1,1,5,5-tetrasubstituted imidosulfamides, according to the scheme

$$2R_2NSO_2NH_2 + OH^- \rightarrow NH_3 + H_2O + (R_2NSO_2NSO_2NR_2)^-,$$

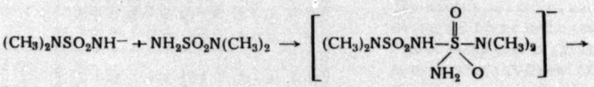
where R can be hydrogen, an alkyl or an aryl.

Using this scheme the sodium salts are obtained in very good yields, and from them the free 1,1,5,5-tetramethylimidosulfamide (I) and 1,5-diphenylimidosulfamide (II). In their chemical properties (I) and (II) are very similar to the unsubstituted imidosulfamide [2]. They represent colorless crystalline compounds, are strong monobasic acids, and when boiled with water for a short time they suffer complete hydrolysis with the formation of the corresponding substituted sulfamines and substituted sulfamic acids. In the case of 1,5-diphenylimidosulfamide the unstable phenylsulfamic acid [4] formed at first is immediately hydrolyzed to aniline acid sulfate

$$C_6H_5NHSO_2NHSO_2NHC_6H_5 \xrightarrow{+H_2O} C_6H_5NHSO_2NH_2 + C_6H_5NHSO_2OH \xrightarrow{+H_2O}$$
$$\rightarrow C_6H_5NH_2 \cdot H_2SO_4 \quad \text{(III)}$$

The formation of (I) and (II) from N,N-dimethylsulfamide and N,N'-diphenylsulfamide shows very clearly that the scheme proposed for the formation of imidosulfamide from sulfamide by treatment of the latter with caustic alkalies [2] is completely incorrect. The formation of (I) makes the following direct scheme more probable

$$(CH_3)_2NSO_2NH_2 + OH^- \rightleftarrows H_2O + (CH_3)_2NSO_2NH^-$$



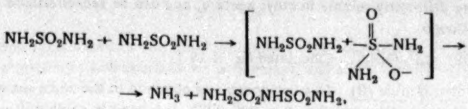
$$(CH_3)_2NSO_2NH^- + NH_2SO_2N(CH_3)_2 \rightarrow \left[(CH_3)_2NSO_2NH-\overset{\overset{\displaystyle O}{\|}}{\underset{\displaystyle NH_2\;\; O}{S}}-N(CH_3)_2 \right]^- \rightarrow$$

$$\rightarrow NH_3 + [(CH_3)_2NSO_2NSO_2N(CH_3)_2]^-$$

The formation of imidosulfamide from sulfamide and tertiary bases can proceed according to the scheme

$$NH_2SO_2NH_2 + Py \rightleftarrows PyH^+ + NH_2SO_2NH^-, \text{ etc.}$$

Since the formation of imidosulfamide, even if only in small yield, is also observed when sulfamide is heated without catalysts, the possibility is not excluded that the initial addition product is formed according to the scheme



$$NH_2SO_2NH_2 + NH_2SO_2NH_2 \longrightarrow \left[NH_2SO_2NH_2^{+}-\overset{O}{\overset{\|}{\underset{NH_2\quad O^-}{S}}}-NH_2 \right] \longrightarrow$$

$$\longrightarrow NH_3 + NH_2SO_2NHSO_2NH_2,$$

and then the reaction is catalyzed by the ammonia, which functions in the same manner as the tertiary bases in the first method for the preparation of imidosulfamide [2]. To be sure, the addition of the hydroxyl ion or of the tertiary bases proceeds much more easily then does that of the weakly basic NH_2 group of sulfamide or of ammonia, and for this reason practically quantitative yields of imidosulfamide are obtained with alkalies, while in the absence of catalysts the yields are quite minute [1].

If these schemes are correct, the substituted imidosulfamides should be obtained from all substituted sulfamides, with the exception of the tetra-substituted. This conclusion is being checked at the present time.

To synthesize other 1,5-disubstituted imidosulfamides it was necessary to obtain the monosubstituted sulfamides of type $RNHSO_2NH_2$. These compounds were obtained by Denivelle [5] and by Battegay and Meybeck [5] by a fairly complicated method, and specifically – by reacting the chlorides of the corresponding N-aryl-N-carboacylsulfamic acids with ammonia, the former being formed by the reaction of sulfuryl chloride with the sodio derivatives of N-arylcarboacylamides [6]. The monomethyl- and monoethylsulfamides were obtained by the hydrolysis of the 3-methyl- and 3-ethylimidosulfamides [3].

Paquin obtained the butyl-, cyclohexyl- and piperidylsulfamides [7] by a simpler process, and specifically – by the reaction of sulfamide with the corresponding amines.

$$RNH_2 + NH_2SO_2NH_2 \longrightarrow NH_3 + RNHSO_2NH_2 \qquad (IV)$$

Paquin makes no mention of obtaining the N-monoarylsulfamides by this scheme; for this reason it was decided to determine if it is possible to obtain N-arylsulfamides by the reaction of aromatic amines with sulfamide. It proved that the aromatic amines readily react with sulfamide when heated on the boiling water bath for several hours, but the yields of monoarylsulfamides and diarylsulfamides formed here are small, which is fully understandable, since the reaction of amines with sulfamide should give, together with the formation of substituted sulfamides, also imidosulfamide, which for all practical purposes is the solitary reaction product when sulfamide is reacted with tertiary amines [2]. In addition, the already formed N-arylsulfamide on heating and reaction with excess ammonia should give the corresponding 1,5-diarylimidosulfamide. Consequently it is impossible to decide at the present time whether the N-arylsulfamides are formed directly from amines and sulfamide by the total scheme (IV) or only as the hydrolysis products of the 1,5-diarylsulfamide found in the reaction mixture according to scheme (III).

EXPERIMENTAL

1,1,5,5-Tetramethylimidosulfamide (I). 0.05 g-mole of 1,1-dimethylsulfamide was added in one portion to 49 ml of vigorously boiling 0.5 N sodium hydroxide solution, contained in an open flask, and the boiling was continued for 10 minutes. Then the solution was cooled rapidly and evaporated to dryness in vacuo on the water bath at 30-35°. The residue, a mass of fine needle crystals, was treated with 5 ml of ethyl alcohol and after good stirring the sodium salt of (I) was suction-filtered, washed with alcohol (3 times with 1-ml portions), and dried in vacuo over sulfuric acid. The sodium salt of (I) is a colorless finely crystalline powder, readily soluble in water, difficultly soluble in alcohol, and insoluble in benzene and ether; yield 88.5%; m.p. 148-150°.

Found %: N 16.33. $C_4H_{12}O_4N_3S_2Na$. Calculated %: N 16.59.

To obtain the free (I), a solution of 0.02 g-mole of the sodium salt of (I) in 5 ml of water, cooled to 0°, was treated under stirring with 1.8 ml of 10 N sulfuric acid solution, also cooled to 0°, and 0.006 g-mole of finely pulverized sulfamic acid. The solution was evaporated in vacuo at 20° to dryness, with the receiver cooled to −20°. The dry crystalline residue was treated with 15 ml of dry acetone, the solution was vacuum-filtered, and the precipitate was washed with acetone (4 times with 5-ml portions). The filtrate was evaporated in vacuo at 20°, and the dry residue was extracted (to remove sulfamic acid) with dry ethyl acetate (2 times with 40-ml portions).

The solution was suction-filtered, the precipitate was washed with ethyl acetate (4 times with 4-ml portions), and the solution was evaporated to dryness in vacuo at 20°. The residue contained (I) as compact colorless prisms; yield 90.9%. After recrystallization from benzene, m.p. 131-133°. (I) is readily soluble in acetone, water and alcohol, somewhat more difficultly soluble in ethyl acetate, and can be recrystallized from benzene. Its water solutions show acid to Congo.

Found %: N 18.09. $C_4H_{13}O_4N_3S_2$. Calculated %: N 18.17.

1,5-Diphenylimidosulfamide (II). This compound was obtained in the same manner as (I). The sodium salt of (II) is a colorless finely crystalline powder, m.p. 206-208°; it is readily soluble in water, very difficultly soluble in alcohol, and insoluble in benzene and ether; yield 90%.

Found %: N 12.20. $C_{12}H_{12}O_4N_3S_2Na$. Calculated %: N 12.03.

The free (II) crystallizes as fine colorless prisms, soluble in benzene, acetone, alcohol and water, and with m.p. 163-165°; yield 87.1%. Its water solutions show acid to Congo.

Found %: N 13.00. $C_{12}H_{13}O_4N_3S_2$. Calculated %: N 12.84.

Hydrolysis of 1,1,5,5-Tetramethylimidosulfamide and 1,5-Diphenylimidosulfamide. A solution of 1 g of (I) in 50 ml of water was boiled for 3 minutes, and after cooling, the solution was extracted 3 times with ether (100, 50 and 50 ml). Removal of the ether by distillation left 1,1-dimethylsulfamide; yield 0.20 g; after recrystallization from benzene, m.p. 94-95°. The compound was identified by its nitrogen content and by mixed melting point.

Properties of Arylsulfamides With Formula $ArNHSO_2NH_2$

Ar	Yield (in %)	Melting point	Crystalline form	Found N (in %)	Empirical formula	Calculated N (in %)
o-$CH_3C_6H_4$	4.6	101-103°	Silvery scales	15.32	$C_7H_{10}O_2N_2S$	15.04
m-$CH_3C_6H_4$	11.8	76-78	Fine needles	14.88	$C_7H_{10}O_2N_2S$	15.04
p-$CH_3C_6H_4$	28.0	123-125	Fine needles	15.21	$C_7H_{10}O_2N_2S$	15.04
o-$CH_3OC_6H_4$	4.9	108-110	Fine prisms	13.99	$C_7H_{10}O_3N_2S$	13.85
p-$C_2H_5OC_6H_4$	4.6	125-126	Long colorless needles	13.15	$C_8H_{12}O_3N_2S$	12.96
m-$NO_2C_6H_4$	9.2	149-150	Prisms	19.49	$C_6H_7O_4N_3S$	19.35
α-$C_{10}H_7$	10.8	129-130	Fine crystalline powder	12.60	$C_{10}H_{10}O_2N_2S$	12.61
β-$C_{10}H_7$	21.1	140-142	Fine crystalline powder	12.80	$C_{10}H_{10}O_2N_2S$	12.61

Also from 1 g of (II) we obtained 0.23 g of phenylsulfamide (m.p. 105-107°); this compound was also identified by its nitrogen content and mixed melting point.

Phenylsulfamide (V). A mixture of 0.05 g-mole of sulfamide and 0.25 g-mole of aniline was heated on the boiling water bath in a flask fitted with a reflux air-condenser; here the liquid gradually separated into layers. Ammonia was slowly evolved. The cooled reaction mixture was treated with 75 ml of 1 N sodium hydroxide solution and 100 ml of ether, and the mixture shaken vigorously. The water solution was separated and then treated with concentrated hydrochloric acid until acid to Congo. Here the diphenylsulfamide deposited as a fine crystalline precipitate, while the phenylsulfamide remained in the water solution. The diphenylsulfamide (VI) was suction-filtered and washed with water (5 times with 5-ml portions), while (V) was extracted from the water solution with ether (5 times with 50-ml portions). The ether extracts were dried over sodium sulfate and the ether was distilled off. The residue contained (V), which was recrystallized from benzene; m.p. 105-107°; colorless lustrous scales. Readily soluble in water, alcohol, acetone and ether.

Found %: N 10.24. $C_6H_8N_2S$. Calculated %: N 10.46.

When the reaction mixture was heated for 2 hours the yield of (V) was 25%, and that of (VI) was 3.8%; when heated for 4 hours, the yield of (V) was 36.4% and that of (VI) was 5.8%; when heated for 6 hours, the yield of (V) was 24.1% and that of (VI) was 5.2%.

The other arylsulfamides (see Table) are obtained in similar manner.

All of the obtained arylsulfamides are readily soluble in acetone, water, alcohol and ether, with the exception of the naphthylsulfamides, which are much more difficultly soluble in water. All of the arylsulfamides were recrystallized from benzene.

SUMMARY

The 1,5-diphenyl- and 1,1,5,5-tetramethylimidosulfamides were synthesized. It was shown that the earlier proposed scheme for the formation of imidosulfamides is incorrect, and a new scheme was proposed. A number of monoarylsulfamides were synthesized.

Received January 17, 1957

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TRICHLOROPHOSPHAZOARYLOXYDICHLOROACETYLS

A. V. Kirsanov and V. P. Molosnova

Recently it was found that the aliphatic esters of oxamic acid react with phosphorus pentachloride, first forming the amides of alkoxydichloroacetic acids [1] according to scheme (I), and then trichlorophosphazoalkoxydichloroacetyls [2] according to scheme (II):

$$ROCOCONH_2 + PCl_5 \rightarrow POCl_3 + ROCCl_2CONH_2 \qquad (I)$$

$$ROCCl_2CONH_2 + PCl_5 \rightarrow 2HCl + ROCCl_2CON{=}PCl_3 \qquad (II)$$

For the aromatic esters of oxamic acid [3] it has been impossible up to now to limit the reaction to scheme (I). Even in the presence of a large excess of the corresponding oxamic acid ester the reaction either does not go, or proceeds immediately according to scheme (III) with the formation of trichlorophosphazoaryloxydichloroacetyls.

$$ArOCOCONH_2 + 2PCl_5 \rightarrow 2HCl + POCl_3 + ArOCCl_2CON{=}PCl_3 \qquad (III)$$

For a possible explanation of this phenomenon see [1].

Under suitable conditions the reaction according to scheme (III) goes either quantitatively or almost quantitatively with the formation of colorless crystals of the trichlorophosphazoaryloxydichloroacetyls (IV). As a rule, the "crude" products melt only several degrees below the recrystallized material, and are usually colorless. Only in the case of the naphthoxy derivatives (XI and XII) are the crude products obtained colored and melt considerably below the pure compounds.

In their physical and chemical properties the (IV) compounds are similar to the trichlorophosphazoalkoxydichloroacetyls [2]. They react violently with water, alcohols, phenols, ammonia, amines and other substances containing active hydrogen atoms. When treated with steam, or even better, with formic acid, the (IV) compounds give in good yields the dichlorides of aryloxydichloroacetamidophosphoric acids (V) according to the scheme

$$ArOCCl_2CON{=}PCl_3 + HCOOH \rightarrow CO + HCl + ArOCCl_2CONHPOCl_2$$

However, in contrast to the trichlorophosphazoalkoxyacetyls, the (IV) compounds are decomposed with much greater difficulty by heat. When heated they do not cleave chlorobenzene and slowly cleave phosphorus oxychloride with much greater difficulty (only at 180°). The (V) compounds are colorless crystalline compounds that melt considerably above the corresponding trichlorophosphazoaryloxydichloroacetyls (IV), and are more difficultly soluble in the common organic solvents than (IV). The (V) compounds react slowly with water at room temperature, and consequently they can be stored without taking any special precautions. When heated with water the (V) compounds are rapidly hydrolyzed, and they react vigorously with compounds containing active hydrogen atoms.

EXPERIMENTAL

All of the solvents and starting substances were carefully dehydrated. All of the operations were run in such manner that both the reaction mixtures and reaction products were exposed to atmospheric moisture as little as possible.

Trichlorophosphazophenoxydichloroacetyl (VI). A mixture of 0.025 g-mole of pulverized phenyl oxamate and 0.05 g-mole of finely divided phosphorus pentachloride was thoroughly mixed in a round-bottomed flask, closed with reflux condenser, which was connected to a gas bubbler containing sulfuric acid and a water trap for collecting hydrogen chloride. The evolution of hydrogen chloride began in 1 to 2 minutes. The flask contents became completely liquid within 10 minutes. The reaction was accompanied by the absorption of heat. In 15--20 minutes, when the evolution of hydrogen chloride had slackened considerably, the flask was immersed in a water bath, heated to 40°. The reaction was ended within 30 minutes. The reaction mixture was cooled and the hydrogen chloride was displaced by dry air. The yield of mixed phosphorus oxychloride and (VI) was quantitative, while the yield of hydrogen chloride was 92%. The phosphorus oxychloride was vacuum-distilled (5 mm) at 20-30° into a receiver cooled to −21°; yield 97%. The residue was crude (VI) as a light yellow turbid liquid; yield 101%. The crude product soon crystallized; m.p. 45° (last crystal, bulb of the thermometer in the liquid). Recrystallization from 10 ml of petroleum ether (b.p. 85-95°) gave the compound as colorless prisms (m.p. 49-50°).

Found %: N 4.00; Cl 49.50, 49.44. Equiv. after hydrolysis 8.13, 8.04. $C_8H_5O_2NPCl_5$. Calculated %: N 3.94; Cl 49.97. Equiv. after hydrolysis 8.00.

The following compounds were obtained in similar manner.

Trichlorophosphazo-o-cresoxydichloroacetyl (VII). The crude product melts at 46°(last crystal). Recrystallization from petroleum ether (85-95°; 2 ml per 0.01 g-mole) gave the compound as coarse colorless prisms (m.p. 49-51°); yield 64%.

Found %: Cl 47.89; P 8.75. Equiv. after hydrolysis 8.02, 8.10. $C_9H_7O_2NPCl_5$. Calculated %: Cl 48.00; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-m-cresoxydichloroacetyl (VIII). The crude product can be recrystallized from a very small volume of petroleum ether (85-95°). Cooling the solution to −10° gave (VIII) as clusters of transparent needles; m.p. 30-34°.

Found %: Cl 47.96, 48.19; P 8.43. Equiv. after hydrolysis 7.99, 7.99. $C_9H_7O_2NPCl_5$. Calculated %: Cl 48.0; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-p-cresoxydichloroacetyl (IX). Crude (IX) melts at 76° (last crystal). Recrystallization from petroleum ether (1 ml per g of compound) gave the compound as long colorless needles (up to 5 mm); m.p. 74-76°.

Found %: N 3.86; Cl 47.86, 47.98; P 8.28. Equiv. after hydrolysis 8.12, 8.18. $C_9H_7O_2NPCl_5$. Calculated %: N 3.79; Cl 48.00; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-p-chlorophenoxydichloroacetyl (X). The reaction was run at 60-75° for 20-25 minutes. Crude (X) melts at 55° (last crystal); recrystallization from petroleum ether (1 ml per 0.01 g-mole) gave the compound as colorless transparent prisms (m.p. 52-55°).

Found %: hydrolyzable Cl 45.57, 45.62; P 8.32. Equiv. after hydrolysis 8.19, 8.22. $C_8H_4O_2NPCl_6$. Calculated %: hydrolyzable Cl 45.48; P 7.95. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-α-naphthoxydichloroacetyl (XI). The reaction was run at 45° for 1 hour. The crude (XI) had a brown color; m.p. 45° (last crystal). After two recrystallizations from either petroleum ether (using each time 8 ml of solvent per 0.01 g-mole of compound) or carbon tetrachloride (0.5 ml per g of substance) the compound was obtained as fine colorless prisms (m.p. 69-72°).

Found %: Cl 43.78; 44.09; P 7.71. Equiv. after hydrolysis 8.22, 8.06. $C_{12}H_7O_2NPCl_5$. Calculated %: Cl 43.74; P 7.64. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-β-naphthoxydichloroacetyl (XII). The reaction was run at 45° for 1 hour. The crude (XII) was colored a light crimson; m.p. 78° (last crystal). Recrystallization from petroleum ether (10 ml per 4 g of substance) gave the compound as colorless needles (m.p. 80-83°); yield 64%.

Found %: Cl 44.06, 44.20; P 7.95. Equiv. after hydrolysis 8.28, 8.20. $C_{12}H_7O_2NPCl_5$. Calculated %: Cl 43.74; P 7.68. Equiv. after hydrolysis 8.00.

All of the (IV) compounds are readily soluble at 20° in acetone, ether and benzene. (VI), (VIII), (IX) and (X) are readily soluble in carbon tetrachloride, while (VII), (XI) and (XII) are difficultly soluble. All of the (IV) compounds are slightly soluble [(X) is somewhat more soluble] in petroleum ether (85-95°) at 20°, while on heating,(XI) and (XII) are readily soluble, and (VI)-(X) are very soluble.

Phenoxydichloroacetamidophosphoryl Dichloride (XIII). To a solution of 0.01 g-mole of (VI) in 15 ml of benzene was added 0.01 g-mole of anhydrous formic acid. A vigorous reaction began immediately with the evolution of hydrogen chloride and carbon monoxide, and (XIII) was deposited as a fine crystalline precipitate, which was suction-filtered, washed with benzene, dried in vacuo, and recrystallized from either 10 ml of petroleum ether (85-95°) or 10 ml of carbon tetrachloride. (XIII) was obtained as colorless transparent prisms; m.p. 155-156°; yield 96%; readily soluble at 20° in dioxan and acetone, and when heated it is soluble in ether, chloroform, dichloroethane, benzene, toluene, carbon tetrachloride and petroleum ether.

Found %: N 4.29; Cl 42.01, 41.97. Equiv. after hydrolysis 7.03, 7.00. $C_8H_6O_3NPCl_4$. Calculated %: N 4.16; Cl 42.09. Equiv. after hydrolysis 7.00.

The following compounds were obtained in similar manner.

o-Cresoxydichloroacetamidophosphoryl Dichloride (XIV). Yield 88%, colorless needles (from benzene); m.p. 128-130°.

Found %: Cl 40.34, 40.24; P 9.57. Equiv. after hydrolysis 7.07, 7.07. $C_9H_8O_3NPCl_4$. Calculated %: Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

m-Cresoxydichloroacetamidophosphoryl Dichloride (XV). Yield 61%, fine needles (from benzene); m.p. 161-163°.

Found %: Cl 40.19, 40.29; P 9.00.Equiv. after hydrolysis 7.08, 7.11. $C_9H_8O_3NPCl_4$. Calculated %: Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

p-Cresoxydichloroacetamidophosphoryl Dichloride (XVI). Yield 98%, slender colorless needles (from benzene); m.p. 144-146°.

Found %: N 3.95; Cl 40.37, 40.38; P 9.12. Equiv. after hydrolysis 7.09, 7.08. $C_9H_8O_3NPCl_4$. Calculated %: N 3.99; Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

α-Naphthoxydichloroacetamidophosphoryl Dichloride (XVII). Yield 34%, aggregates of needles resembling snowflakes (from benzene); m.p. 140-142°.

Found %: Cl 36.56; P 8.00. Equiv. after hydrolysis 7.06, 7.03. $C_{12}H_8O_3NPCl_4$. Calculated %: Cl 36.67; P 8.01. Equiv. after hydrolysis 7.00.

β-Naphthoxydichloroacetamidophosphoryl Dichloride (XVIII). Yield 60%, colorless needles (from benzene); m.p. 163-165°.

All of the (V) compounds are readily soluble in acetone, difficultly soluble in cold benzene, and readily soluble in boiling benzene. (XVI) is readily soluble in ether, (XIV), (XVII) and (XVIII) are difficultly soluble, and (XV) is very difficultly soluble. (XIV)-(XVI) are difficultly soluble in carbon tetrachloride and petroleum, while (XVII) and (XVIII) are very difficultly soluble.

SUMMARY

Some trichlorophosphazoaryloxydichloroacetyls and dichlorides of aryloxydichloroacetamidophosphoric acids were synthesized.

Received January 17, 1957

Dnepropetrovsk Metallurgical Institute

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REACTION OF TETRAFLUOROETHYLENE WITH ARSENIC TRICHLORIDE IN THE PRESENCE OF ALUMINUM CHLORIDE

A. B. Bruker, T. G. Spiridonova and L. Z. Soborovskii

In recent years the reaction of tetrafluoroethylene with a whole series of different compounds has been accomplished; with halides, hydrogen halides, sulfur chloride, nitrogen dioxide, ammonia, amines, alcohols, glycols, alkyl halides, mercaptans, hydroxy mercaptans, ethylene, acrolein, acrylonitrile, vinyl chloride, etc. [1]. Despite the large number of reactions described, up to now only a very few examples are known of the reaction of tetrafluoroethylene with metal halides and the preparation of perfluoroorganometallic compounds.

The reaction of arsenic trichloride with tetrafluoroethylene wasstudied in the present paper. The reaction of arsenic trichloride .with unsaturated compounds has been extensively studied only in the case of reaction with acetylene [2-7]. The reaction with ethylene has been studied to a lesser degree. Renshaw and Ware [8] and the Nekrasovs [9] have shown that the saturation of arsenic trichloride with ethylene in the presence of anhydrous aluminum chloride at atmospheric pressure and room temperature results in the formation of β-chloroethyldichloroarsine in low yield.

We first attempted to react tetrafluoroethylene with arsenic trichloride under conditions similar to those used in the reaction with ethylene, i.e., by saturating arsenic trichloride with tetrafluoroethylene in the presence of aluminum chloride at atmospheric pressure. The results were negative; we were unable to isolate any organoarsenic compounds here. Equally unsuccessful were the experiments run in an autoclave under pressure, but without the aluminum chloride. On making a more detailed study of this reaction it was established by us that when arsenic trichloride is reacted with tetrafluoroethylene in the presence of aluminum chloride in a rotating autoclave at 70--90° for 9-12 hours the main product in the obtained reaction mixture is a substance containing carbon, fluorine, chlorine and arsenic. Based on the analysis data, molecular weight and molecular refraction, and also based on the analysis of the transformation and decomposition products, the substance was identified as being the previously unknown pentafluoroethyldichloroarsine. The substance is a colorless liquid with b.p. 86-87°, with the sharp odor characteristic of arsine chlorides. Besides pentafluoroethyldichloroarsine, we isolated a second substance from the reaction mixture – a colorless liquid with b.p. 20-21°. This substance decolorized bromine water; based on the analysis data, molecular weight and boiling point, and also based on the physicochemical properties of the bromide obtained from it, this substance corresponds to the known 1,1-difluoro-2,2-dichloroethylene [10].

The described reaction can be depicted by the following scheme.

$$3CF_2{=}CF_2 + 2AsCl_3 \xrightarrow{AlCl_3} 2CF_3CF_2AsCl_2 + CF_2{=}CCl_2 \qquad (1)$$

The yield of pentafluoroethyldichloroarsine based on reacted arsenic trichloride was 70%, and based on tetrafluoroethylene taken for reaction it was 50-60% of the theoretical [in accordance with equation (1)].

The formation of pentafluoroethyldichloroarsine as the result of Reaction (1), instead of the expected tetrafluoro-β-chloroethyldichloroarsine, indicated that this process is different from the usual reaction for the addition of arsenic trichloride to unsaturated compounds. The explanation for this peculiar behavior should be sought in the ability shown by aluminum chloride to exchange its chlorine for fluorine when reacted with fluorinated hydrocarbons [11-15]. It seems probable that also in the discussed case the first reaction to take place is exchange of halogen between tetrafluoroethylene and aluminum chloride.

$$CF_2{=}CF_2 + AlCl_3 \rightarrow AlF_2Cl + CF_2{=}CCl_2 \qquad (2)$$

Evidence in support of this is the fact that in all of the experiments the amount of difluorodichloroethylene isolated, together with pentafluoroethyldichloroarsine, corresponded to the ratio shown by Equation (1). Subsequent reaction of the tetrafluoroethylene with arsenic trichloride and aluminum difluorochloride results in the formation of pentafluoroethyldichloroarsine and aluminum fluorodichloride, both of which are present in the reaction mixture.

$$CF_2{=}CF_2 + AlF_2Cl + AsCl_3 \xrightarrow{AlCl_3} CF_3CF_2AsCl_2 + AlFCl_2 \qquad (3)$$

The aluminum fluorodichloride formed in this manner can also react with tetrafluoroethylene, again yielding aluminum difluorochloride.

$$CF_2{=}CF_2 + 2AlFCl_2 \longrightarrow CF_2{=}CCl_2 + 2AlF_2Cl \qquad (4)$$

The presented schemes satisfactorily explain the fact that comparatively small amounts of aluminum chloride are sufficient for the transformation of substantial amounts of tetrafluoroethylene to pentafluoroethyldichloroarsine and difluorodichloroethylene (see Table).

Reaction of Tetrafluoroethylene With Arsenic Trichloride in the Presence of Aluminum Chloride

Change (in g)			Temperature (in autoclave)	Reaction time (in hours)	Weight of obtained reaction mass (in g)	Fractions isolated (in g)		Analysis of $C_2F_5AsCl_2$ (in %)		Yield based on $CF_2{=}CF_2$ (in % of theoretical)*	
$AsCl_3$	$AlCl_3$	$CF_2{=}CF_2$				b.p. 20-21°	b.p. 86-87°	As	Cl	$C_2F_5AsCl_2$	$C_2F_2Cl_2$
365	8.8	44	70—80°	18	386.5	11.7	34.5	27.25	26.35	44.4	60.6
252.2	8.1	24	70	9	254.5	6.2	20.5	26.4	25.8	48.3	59.0
253.1	9.4	22	70	9	274.8	6.7	20.4	27.0	27.0	52.5	69.7
142.5	7.1	13	90—125	12	159.9	3.7	11.3	25.8	25.0	49.3	64.9
254	9.0	73.6	50—70	21	300	19.3	56.4	26.6	25.8	43.3	59.0
255	5.75	20	80—100	40	267.1	6.0	18.0	26.05	24.7	50.9	68.0

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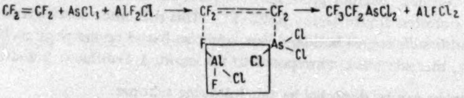
* The yield was calculated according to Equation (1) without considering the pentafluoroethyldichloroarsine contained in the intermediate fractions.

The described process can be depicted by the following general scheme, postulating the formation of an intermediate complex, the decomposition of which leads to the formation of pentafluoroethyldichloroarsine and aluminum fluorodichloride.



The presence of 1,1-difluoro-2,2-dichloroethylene in the reaction mixture in amounts corresponding to Equation (1) indicates that under the described conditions this compound is practically inert toward arsenic trichloride, present in excess. This is also supported by the fact that we were unable to find any other organoarsenic compounds besides pentafluoroethyldichloroarsine in the reaction products.

A study of the properties of the obtained pentafluoroethyldichloroarsine revealed that this compound is easily decomposed by aqueous alkali solutions in the cold with a nearly quantitative evolution of pentafluoroethane, which is additional evidence that this compound has the structure of pentafluoroethyldichloroarsine. The oxidation of pentafluoroethyldichloroarsine with hydrogen peroxide in the cold gave pentafluoroethylarsonic acid. The silver salt of the acid was obtained as white scales with a mother-of-pearl luster. The reduction of pentafluoroethylarsonic acid with sulfur dioxide in hydrochloric acid medium gave pentafluoroethyldichloroarsine, identical with the product isolated in the reaction of tetrafluoroethylene with arsenic trichloride. The heating of pentafluoroethyldichloroarsine with ammonium fluoride at 70° gave pentafluoroethyldifluoroarsine as a colorless liquid, boiling at 47-48°, and having a sharp odor. The reduction of pentafluoroethyldichloroarsine with zinc in alcohol-hydrochloric acid medium gave pentafluoroethylarsine, obtained as a colorless transparent liquid with b.p. 27-28°.

EXPERIMENTAL

1. Reaction of Tetrafluoroethylene With Arsenic Trichloride in the Presence of Aluminum Chloride. Into a 500-ml, rotated, stainless steel autoclave, fitted with thermocouple well, valve, manometer and safety disc, was charged 250-300 g of freshly distilled arsenic trichloride and 7-9 g of freshly sublimed aluminum chloride. After this the air was removed from the autoclave by means of a vacuum-pump to a vacuum of 4-5 mm. To remove the last traces of air the autoclave was blown with tetrafluoroethylene and then filled with the same gas to a pressure of 9-14 atm., which corresponded to 16-30 g of C_2F_4. During the first 5 hours the autoclave was rotated without heating, and then the electrical heat was turned on; the temperature in the autoclave was gradually raised to 70-90°. The autoclave was rotated at this temperature for 9-12 hours. The pressure at the end of reaction usually dropped to atmospheric.

The reaction mass unloaded from the autoclave was fractionally distilled. After 2-3 distillations in a CO_2 atmosphere we isolated, besides unreacted arsenic trichloride, two fractions:

1st Fraction with b.p. 20-21° was 1,1-difluoro-2,2-dichloroethylene.

Found M 138. $C_2F_2Cl_2$. Calculated M 133.

Bromination of the obtained difluorodichloroethylene gave the dibromide with b.p. 138-139° and m.p. 45°, corresponding to 1,1-difluoro-2,2-dichloro-1,2-dibromoethane (according to the literature data [10]: b.p. 138.8-139°, m.p. 45.5°).

Found %: F 12.0; Cl + Br (calculated as Cl) 48.3. $C_2F_2Cl_2Br_2$. Calculated %: F 12.9; Cl + Br 48.4.

2nd Fraction with b.p. 86-87° was a colorless transparent liquid with a sharp odor, and was pentafluoroethyldichloroarsine.

d^{20}_4 1.9221, $n^{20}D$ 1.4063, MR_D 33.56; calc. 33.56.

Found %: As 28.8; Cl 26.55; F 34.9; C 9.55. M 260. $C_2F_5Cl_2As$. Calculated %: As 28.3; Cl 26.7; F 35.6; C 9.0. M 265.

The distillation residue, a grayish viscous mass, was treated with concentrated hydrochloric acid. Evaporation of the solution gave a residue from which the hydrate of aluminum fluorodichloride, corresponding to the composition $AlFCl_2 \cdot 6H_2O$, was isolated.

Found %: F 7.3; Cl 32.1; Al 11.9. $AlFCl_2 \cdot 6H_2O$. Calculated %: F 8.4; Cl 31.5; Al 12.0.

The results of the experiments, run under various conditions, are given in the Table.

From the data given in the table it follows that the optimum reaction conditions are a time of 9-12 hours at 70-90° and molar ratios $AsCl_3 : C_2F_4 : AlCl_3 = 1.39 : 0.22 : 0.07$. An increase in the amount of aluminum chloride, and also the reaction time, do not affect the yield of pentafluoroethyldichloroarsine.

2. Decomposition of Pentafluoroethyldichloroarsine With Alkali Solution. A solution of potassium hydroxide (8 g of KOH in 76 ml of water) was placed in a flask, fitted with dropping funnel and connected to a trap, cooled to −80°. 10 g of pentafluoroethyldichloroarsine was added gradually from the dropping funnel. Here 4 g of a clear colorless liquid condensed in the trap, which when fractionally distilled through a Podbelniak column almost completely distilled at −49 to −49.5° (pentafluoroethane has b.p. −48.5° [16]).

Found %: C 20.9. M 122.4. C_2F_5H. Calculated %: C 20.0. M 120.0.

3. Oxidation of Pentafluoroethyldichloroarsine to Pentafluoroethylarsonic Acid. Into a 100-ml flask was charged 20.2 g of pentafluoroethyldichloroarsine and 20 ml of water. Then 26 g of aqueous hydrogen peroxide solution (14.7% H_2O_2) was added gradually at 1-2°. The water was vacuum-distilled. The residue was washed with benzene and dried at 100° to constant weight. The acid was obtained as a fine crystalline powder. The silver salt of the acid was obtained as white scales with a mother-of-pearl luster.

Found %: As 16.5; F 22.1; Ag 47.4. $C_2F_5O_3Ag_2As$. Calculated %: As 16.4; F 20.75; Ag 47.1.

4. Converstion of Pentafluoroethylarsonic Acid to Pentafluoroethyldichloroarsine. Four grams of pentafluoroethylarsonic acid was mixed with 20 ml of hydrochloric acid (1 : 1), a crystal of potassium iodide was added, and then sulfur dioxide was passed through the mixture for 30 minutes. The reaction product was separated from the aqueous layer, dried over sodium sulfate, and then distilled. We isolated 1 g of substance with b.p. 86-87°.

Found %: As 27.8; Cl 26.3. $C_2F_5Cl_2As$. Calculated %: As 28.3; Cl 26.7.

5. Preparation of Pentafluoroethyldifluoroarsine. Into a distilling flask, fitted with Vigreux column and descending condenser, was charged 5.9 g of pentafluoroethyldichloroarsine and 2.5 g of ammonium fluoride. The flask contents were heated on the water bath, the temperature of which was gradually raised to 70°; here 2 g of a clear colorless liquid with a sharp odor was obtained as distillate, which after redistillation had the following constants.

B. p. 47-48°, d^{20}_4 2.0754, $n^{20}D$ 1.3472, MR_D 23.73; calc. 23.03.

Found %: As 31.65; F (hydrolyzable) 15.8. M 232. C_2F_7As. Calculated %: As 32.3; F (hydrolyzable) 16.3. M 232.

6. Preparation of Pentafluoroethylarsine. Into a round-bottomed flask, fitted with reflux condenser and two dropping funnels, was charged 10-12 g of granulated zinc. A mixture of 50 ml of concentrated hydrochloric acid and 25 ml of methanol was placed in one dropping funnel, and a mixture of 26 g of pentafluoroethyldichloroarsine and 25 ml of methanol was placed in the other. The hydrochloric acid-alcohol mixture and the alcohol solution of pentafluoroethyldichloroarsine were added alternately to the flask with zinc. Here the flask contents became quite hot. The gases escaping from the flask, after being washed in two water towers and dried over calcium chloride, entered a trap cooled to −50°. 7.5 g of a clear colorless liquid condensed in the trap, which was distilled in a stream of CO_2; b.p. 26-27°, $n^{20}D$ 1.331.

Found %: As 37.0; F 47.9. M 208.7. $C_2H_2F_5As$. Calculated %: As 38.2; F 48.4. M 196.0.

SUMMARY

1. Tetrafluoroethylene was made to react with arsenic trichloride in the presence of aluminum chloride at elevated temperature and under pressure, and some concepts were expressed regarding the mechanism of this process. The previously unknown pentafluoroethyldichloroarsine was isolated as the main reaction product.

2. The previously unknown pentafluoroethyldifluoroarsine, pentafluoroethylarsine and pentafluoroethylarsonic acid were synthesized and characterized.

Received February 2, 1957.

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STRUCTURE AND CHEMICAL TRANSFORMATIONS OF ALKALI-ORGANIC COMPOUNDS OF ANILS

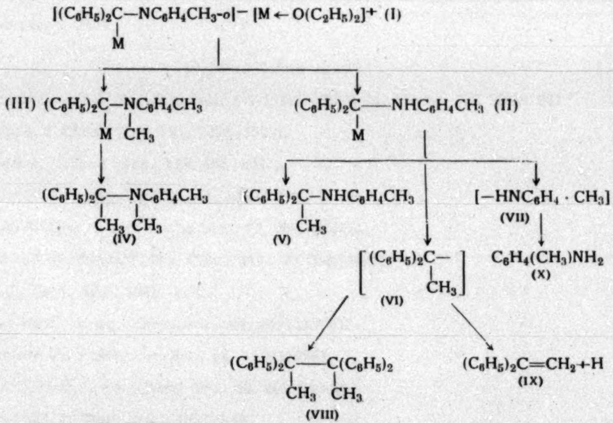
III. TRANSFORMATIONS OF DISODIUM AND DILITHIUM COMPOUNDS OF BENZOPHENONE-o-TOLYLIMIDE AND BENZOPHENONE-p-TOLYLIMIDE UNDER THE INFLUENCE OF ALKYL HALIDES

B. M. Mikhailov and K. N. Kurdiumova

In the previous communication [1] it was shown that complex transformations occur when alkyl halides are reacted with dimetallic compounds of benzophenonephenylimide. The products formed as a result of these transformations are phenylbenzhydrylamine, the product of replacing both of the atoms of the alkali metal by hydrogen atoms, and a number of substances that arise as the result of the molecules decomposing at the carbon—nitrogen bond, namely aniline, phenylated ethylenic hydrocarbons, 2,2,3,3-tetraphenylbutane (when a methyl halide is used), and also gaseous hydrocarbons.

To determine the influence exerted by the structure of the aryl radical on the nitrogen atom on the reaction course of dimetallic compounds of anils we studied the reaction of methyl chloride and iodide with the disodium and dilithium compounds of benzophenone-o-tolylimide and benzophenone-p-tolylimide $(C_6H_5)_2C=NC_6H_4CH_3$-(o- or p-) · $2M(C_4H_{10}O)$ (M = Na or Li).

A complex reaction is observed when the dilithium compound of benzophenone-o-tolylimide is reacted with methyl iodide, leading to the formation of various substances. The collective transformations can be depicted by the following scheme



M = Na, Li

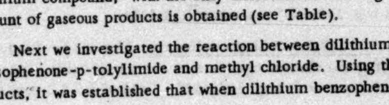
Reaction Products of Dimetallic Compounds $(C_6H_5)_2C=NC_6H_4CH_3$-(o- or p-) · $2M(C_4H_{10}O)$ (From 20 g of Anil) With Alkyl Halides

Starting compounds			Obtained (in %)					Amount of gas (in ml)
dimetallic compound		alkyl halide	$(C_6H_5)_2C(CH_3)-N(CH_3)C_6H_4CH_3$ (IV)	$(C_6H_5)_2C(CH_3)-NHC_6H_4CH_3$ (V)	$C_6H_4(CH_3)NH_2$ (X)	$(C_6H_5)_2C=CH_2$ (IX)	$(C_6H_5)_2C(CH_3)-C(CH_3)(C_6H_5)_2$ (VIII)	
position of CH_3 group in tolyl radical	metal							
Ortho	Li	CH_3I	8.0	15.0	30.7	29.0	6.0	162
Ortho	Na	CH_3I	4.0	16.0	32.0	30.0	10.6	967
Para	Li	CH_3Cl	20.8	—	57.6	33.8	8.0	82
Para	Na	CH_3I	28.8	—	41.7	33.8	3.0	800

The starting dimetallic compound (I) apparently has the same structure as the dimetallic compound of benzophenone-phenylimide. In the proposed scheme it is assumed that the atoms of the metal react in sequence, in which connection the ionized atom of the metal reacts first [2]. The difference between the discussed scheme for the transformations of the dimetallic compounds of benzophenonephenylimide homologs and the scheme for the transformations of the dimetallic compounds of benzophenonephenylimide itself consists in the fact that compound (I) in the first phase of reaction is not only capable of replacing the ionized atom of the metal by hydrogen with the formation of (II), but is also capable of replacing the ionized atom by a hydrocarbon radical with the formation of a monometallic compound (III), which then exchanges the metal for a methyl group and is converted to the tertiary amine – the N-methyl-1,1-diphenylethylamine (IV).

Compound (II) does not undergo reduction, as is observed in the benzophenonephenylimide series, but instead exchanges the metal for the methyl group and in this connection partially retains the anil skeleton, being converted to N-(o-tolyl)-1,1-diphenylethylamine (V), and in part suffers decomposition at the C—N bond with the formation of radicals (VI) and (VII). Further transformations of the latter are analogous to the transformations of the radicals obtained from the dimetallic compounds of benzophenonephenylimide itself, and lead to the formation of 1,1-diphenylethylene (IX), 2,2,3,3-tetraphenylbutane (VIII) and o-toluidine (X) (see Table).

N-(o-Tolyl)-1,1-diphenylethylamine (V) and N-methyl-N-(o-tolyl)-1,1-diphenylethylamine (IV) were obtained as a mixture, for the separation of which we used a new method of separating amines, based on the metalation reaction. This method consists in selective reaction with butyllithium, where the secondary amine (V) is converted to the lithium amide and is isolated from the solution (using a suitable solvent), while the tertiary amine (IV) remains unchanged in the solution. N-(o-Tolyl)-1,1-diphenylethylamine (V) was identified by comparing it with the synthetic specimen, obtained by the addition of phenyllithium to acetophenone-o-tolylimide and subsequent hydrolysis of the lithium derivative.



$$\underset{\displaystyle CH_3}{C_6H_5C}=NC_6H_4CH_3+C_6H_5Li\rightarrow$$

$$\rightarrow(C_6H_5)_2\underset{\displaystyle CH_3}{C}-\underset{\displaystyle Li}{N}C_6H_4CH_3\rightarrow(C_6H_5)_2\underset{\displaystyle CH_3}{C}-NHC_6H_4CH_3$$

The behavior of the disodium compound of benzophenone-o-tolylimide toward methyl iodide is similar to that of the dilithium compound, with the only difference that a large amount of gaseous products is obtained (see Table).

Next we investigated the reaction between dilithium benzophenone-p-tolylimide and methyl chloride. Using the above described method of analyzing the reaction products, it was established that when dilithium benzophenone-

-p-tolylimide is reacted with methyl chloride, of the compounds retaining the skeleton of the original molecule, only the tertiary amine – N-methyl-N-(p-tolyl)-1,1-diphenylethylamine – is formed. Besides this compound, the other products formed during reaction are p-toluidine, 1,1-diphenylethylene and 2,2,3,3-tetraphenylbutane (see Table). The amount of gaseous products obtained was small. The reaction between disodium benzophenone-p-tolylimide and methyl iodide proceeds in a similar manner. The same compounds are obtained as with methyl chloride, but in somewhat different proportions.

The transformations of the dimetallic compounds of benzophenone-p-tolylimide can be depicted by the above described scheme with the difference that in this case the compound, corresponding to compound (V), is not obtained, while the monometallic compound of type (II), exchanging the metal for the methyl group, suffers only decomposition at the C–N bond with the formation of 1,1-diphenylethyl radicals (IV) and a radical similar to (VII).

EXPERIMENTAL

The dimetallic compounds of benzophenone-o-tolylimide and benzophenone-p-tolylimide were obtained using the conditions described for the preparation of the organometallic compounds of benzophenonephenylimide [1].

Reaction of Dilithium Benzophenone-o-tolylimide With Methyl Iodide. The reaction between methyl iodide (11.4 g) and dilithium benzophenone-o-tolylimide, obtained from 20 g (0.07 g-mole) of anil and 1.62 g (0.23 g-atom) of lithium in 200 ml of absolute ether, was run under the conditions described earlier for the reaction of disodium benzophenonephenylimide with methyl iodide [2]. The compounds obtained from the reaction are described below.

1. N-Methyl-N-(o-tolyl)-1,1-diphenylethylamine and N-(o-tolyl)-1,1-diphenylethylamine were isolated as a water-insoluble mixture of amine hydrochlorides (5.45 g). The hydrochlorides of the amines were converted to the free base by treatment with 10% alcoholic NaOH solution. The obtained oily product was vacuum-distilled at 192-212° (10 mm) to give a viscous yellow oil, which partially crystallized on standing. To separate the secondary and tertiary amines, 1 g of the oily product with b.p. 195-212° (10 mm) was dissolved in 50 ml of petroleum ether; the solution was placed in a Dewar ampul, and then treated with a solution of butyllithium in petroleum ether (6 ml, 0.01 mole). The resulting precipitate of lithium amide was filtered on a special filter in a nitrogen atmosphere and then vacuum-dried. We obtained 0.65 g of the lithium amide, which after treatment with methanol gave 0.5 g of substance with m.p. 96-99°, after recrystallization from methanol having m.p. 99.5-101°.

Found %: C 87.76; H 7.49. $C_{21}H_{21}N$. Calculated %: C 87.76; H 7.40.

The substance does not depress the melting point when mixed with a specimen of the N-(o-tolyl)-1,1-diphenylethylamine obtained from acetophenone-o-tolylimide and phenyllithium.

The filtrate after removal of the lithium amide was worked up to yield 0.35 g of an oily substance, which crystallized on standing. After recrystallization from methanol the substance had m.p. 110-112° and was the tertiary amine – N-methyl-N-(o-tolyl)-1,1-diphenylethylamine (IV).

Found %: C 87.44; H 7.53. $C_{22}H_{23}N$. Calculated %: C 87.66; H 7.69.

The hydrochloride of N-methyl-N-(o-tolyl)-1,1-phenylethylamine crystallizes from acetone as slender needles, m.p. 215-216°.

2) o-Toluidine. The hydrochloric acid solution, obtained after treating the reaction products with hydrochloric acid, was made alkaline, and the oil extracted with benzene and then distilled. We obtained 2.4 g (30%) of o-toluidine, b.p. 62-63° (2 mm), d^{20}_4 0.9936, $n^{20}D$ 1.5686.

3) 1,1-Diphenylethylene. The benzene extract, obtained after treating the reaction products with hydrochloric acid, was evaporated and the residue was fractionated. We obtained 3.8 g (29.0%) of 1,1-diphenylethylene with b.p. 102-105° (2 mm), $n^{20}D$ 1.6084.

4. 2,2,3,3-Tetraphenylbutane. The residue from the distillation of the 1,1-diphenylethylene in an amount of 2.8 g was chromatographed on aluminum oxide. Petroleum ether was used for the elution. We obtained 0.8 g of substance with m.p. 126-127°. Yield of 2,2,3,3-tetraphenylbutane was 6%.

In this experiment we obtained 162 ml of gas with the following composition (in %): acetylene 3.88, propylene + + butylene 1.48, ethylene 4.44, hydrogen 4.63, higher hydrocarbons 4.63, methane 80.9.

Acetophenone-o-tolylimide. A mixture of 18 g (0.5 g-mole) of acetophenone acetal [3] and 10.7 g (1 g--mole) of o-toluidine was boiled under reflux for 45 minutes, and then the reaction product was distilled at 157-159° (6 mm). We obtained 8.08 g of acetophenone-o-tolylimide, which after recrystallization from petroleum ether and ethanol had m.p. 59-60°, which agrees with the literature [4]. The yield of the anil was 40%.

N-(o-Tolyl)-1,1-diphenylethylamine (from acetophenone-o-tolylimide and phenyllithium). A solution of 7.0 g (0.03 g-mole) of acetophenone-o-tolylimide in 30 ml of absolute ether was placed in a nitrogen-filled Dewar ampul, and then an ether solution of phenyllithium (43.3 ml of an 0.116 N solution) was added. The ampul was sealed and heated for 3 hours at 35-40°. Then the reaction mass was treated with methanol and water. The residue, obtained from the ether solution, was vacuum-distilled. We obtained 2.4 g of a viscous yellow oil with b.p. 200-210° (7 mm), which immediately crystallized when rubbed with petroleum ether, m.p. 99-101°. Recrystallization from methanol gave the compound as colorless prisms, m.p. 99.5-101°.

Found %: C 87.56; H 7.36. $C_{21}H_{21}N$. Calculated %: C 87.76; H 7.40.

SUMMARY

1. The presence and position of a methyl group in the aryl radical on the nitrogen atom of the azomethine bond exerts substantial influence on the reaction course when methyl halides are reacted with the dimetallic derivatives of benzophenone-o-tolylimide and benzophenone-p-tolylimide.

2. The dimetallic derivatives of benzophenone-o-tolylimide when reacted with methyl iodide are capable of replacing the atoms of the metal by methyl groups with the formation of the secondary amine – N-(o-tolyl)--1,1-diphenylethylamine – and the tertiary amine – N-methyl-N-(o-tolyl)-1,1-diphenylethylamine. Simultaneously with the formation of the amines, cleavage of the azomethine bond in the dimetallic derivative is observed and the formation of o-toluidine, 1,1-diphenylethylene and 2,2,3,-tetraphenylbutane.

3. The reaction of a methyl halide with the dimetallic derivatives of benzophenone-p-tolylimide proceeds with the simultaneous formation of the tertiary amine – N-methyl-N-(p-tolyl)-1,1-diphenylethylamine – and the cleavage of the C–N bond in the dimetallic compound with the formation of p-toluidine, 1,1-diphenylethylene and 2,2,3,3-tetraphenylbutane.

Received April 20, 1957

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*Original Russian pagination. See C. B. Translation.

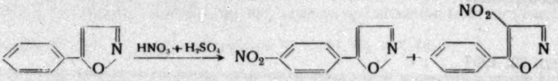
ISOXAZOLE DERIVATIVES

V. SUBSTITUTION IN 5-PHENYLISOXAZOLE

N. K. Kochetkov and E. D. Khomutova

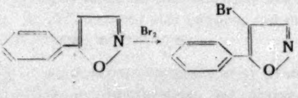
Although oxazole derivatives were discovered in 1888, relatively few members of this class of compounds are known. It is known that individual members of this class of compounds can be nitrated [1], halogenated [2], and sulfonated [3]. However, the position held by isoxazole in the aromatic series of compounds has not been established up to now. The activity of the isoxazole nucleus in substitution reactions when compared with other aromatic systems has also not been investigated. We undertook a study of the activity of the isoxazole nucleus in electrophilic substitution reactions, such as nitration and halogenation, and also in the mercuration reaction. It seemed of interest to determine the activity of the isoxazole nucleus in comparison, for example, to the benzene ring. As the first example we chose the earlier slightly studied 5-phenylisoxazole.

5-Phenylisoxazole was synthesized by the earlier described method [4] from phenyl β-diethylaminovinyl ketone and hydroxylamine hydrochloride in methanol. The nitration of 5-phenylisoxazole with a mixture of nitric and sulfuric acids under cooling gave in a total yield of 75% a mixture of nitro products, which contained 45% of 5-(p-nitrophenyl)isoxazole, identical with the substance obtained from p-nitrophenyl β-chlorovinyl ketone and hydroxylamine hydrochloride [4], and 30% of a nitro-5-phenyloxazole, the oxidation of which with potassium permanganate resulted in the isolation of benzoic acid.

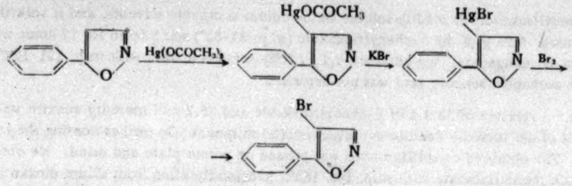


In addition to the two products indicated above, the reaction mixture contained a certain amount (15% of the total amount of reaction products) of unidentified substance, which apparently is a mixture of polynitro derivatives and destruction products.

The bromination of 5-phenylisoxazole was run under the same conditions as for the bromination of benzene, i.e., using iron catalyst and with heating. Here a 70% yield of bromo-5-phenyloxazole was obtained, the oxidation of which with potassium permanganate gave benzoic acid in 74% yield, which indicates the impossibility of having a second isomer (the product of bromination in the phenyl nucleus) present in any substantial amount.



The mercuration of 5-phenylisoxazole with mercury acetate proceeds under milder conditions than does the mercuration of benzene [5] and gives 5-phenylisoxazole mercuriacetate in 90% yield, in which connection only the isoxazole nucleus is mercurated. The 5-phenylisoxazole mercuriacetate was converted to the corresponding bromide, the bromination of which gave a product identical with the compound obtained by the direct bromination of 5-phenylisoxazole. The yields of the mercuribromide derivative and bromo-5-phenylisoxazole are quite great (respectively 98 and 68%), and consequently it is difficult to assume that any substantial amounts of phenyl-mercurated products are formed here.



As a result, if in nitration the degree of substitution in the phenyl and in the oxazole ring is approximately the same, then in bromination and mercuration the substitution is exclusively in the isoxazole ring. It should be mentioned that the nitration and mercuration of 5-phenylisoxazole proceed under milder conditions than is the case for the analogous reactions with benzene. Bromination, proceeding under the same conditions as for the bromination of benzene, is exclusively in the isoxazole ring. All of this suggests that of the two rings found in 5-phenyloxazole, it is the isoxazole ring that is the more active.

The position of the substituents in the isoxazole ring of the 5-phenylisoxazole derivatives obtained by us is being worked upon at the present time, and as indicated above, there is basis to assume that the substituents are found in the 4-position.

EXPERIMENTAL

Nitration. Nine grams of 5-phenylisoxazole was added with vigorous stirring and cooling at −10 to −5° to 30 ml of sulfuric acid (d 1.83). To the obtained mass with cooling from −5 to −2° was added a mixture of 14 ml of nitric acid (d 1.54) and 20 ml of sulfuric acid (d 1.83), after which the reaction mixture was stirred at 15-18° for 1 hour and then poured on ice. The obtained white crystals were filtered, washed with water, and dried in a vacuum-desiccator over phosphorus pentoxide. We obtained 8.85 g of substance (75% yield) with m.p. 95-120°. Recrystallization from methyl alcohol gave 4 g (45%) of colorless crystals with m.p. 163-165°. After 2 recrystallizations from methyl alcohol the compound was obtained as colorless needle crystals with m.p. 171-172°.

Found %: N 14.75, 14.86. $C_9H_6O_3N_2$. Calculated %: N 14.73.

The mixed melting point with the substance obtained from p-nitrophenyl β-chlorovinyl ketone, was not depressed.

5-(p-Nitrophenyl)isoxazole (m.p. 171-172°) was heated for 10 hours with a water solution of potassium permanganate. p-Nitrobenzoic acid with m.p. 233° was obtained; after recrystallization from water, m.p. 237-237.5° (238° [6]). The mixed melting point with authentic p-nitrobenzoic acid was not depressed.

The mother liquor from the recrystallization of the product with m.p. 95-120° was evaporated in vacuo, the obtained crystals were filtered, and 2.7 g of substance (30% of the total amount of reaction products) with m.p. 107-109° was isolated. Evaporation of the filtrate gave 1.5 g of yellow oil, which partially crystallized on long standing. After 3 recrystallizations from methyl alcohol the compound was obtained as white crystals with m.p. 115.5-116.5°.

Found %: C 56.93, 57.16; H 3.10, 3.12. $C_9H_6O_3N_2$. Calculated %: C 56.84; H 3.15.

Nitro-5-phenylisoxazole (m.p. 115.5-116.5°) was heated for 8 hours with a water solution of potassium permanganate, and benzoic acid with m.p. 125-126° was isolated; after precipitation from the salt and recrystallization from water the compound was obtained as lustrous white crystals with m.p. 122° (122° [7]). The mixed melting point with authentic benzoic acid was not depressed.

Bromination. To a suspension of 0.1 g of iron powder in 10 g of 5-phenylisoxazole was added 11 g of bromine in drops; slight warming up of the mixture was observed. The mixture was heated on the boiling water bath until the evolution of hydrogen bromide ceased, and then it was dissolved in ether. The ether solution was washed with aqueous sodium thiosulfate solution, then with water, and the ether was evaporated in the cold; the crystals were dried over phosphorus pentoxide; yield 10.5-10.8 g (68-70%). Two recrystallizations from petroleum ether gave the compound as colorless plates with m.p. 31-32°.

Found %: C 48.37, 48.17; H 2.61, 2.68. C_9H_6ONBr. Calculated %: C 48.24; H 2.69.

Bromo-5-phenylisoxazole is readily soluble in the common organic solvents, and is volatile with steam. B.p. 101-102° (1 mm). 0.25 g of the 5-phenylisoxazole (m.p. 31-32°) was heated for 12 hours with a water solution of potassium permanganate. We obtained 0.1 g (74%) of benzoic acid with m.p. 121-122°. The mixed melting point with authentic benzoic acid was not depressed.

Mercuration. A mixture of 13.4 g of 5-phenylisoxazole and 28.2 g of mercury acetate was heated on the water bath until all of the mercury acetate had dissolved (30 minutes). On further heating the reaction mass crystallized completely. The obtained crystalline mass was pressed on porous plate and dried. We obtained 33.9 g (90%) of 5-phenylisoxazole mercuriacetate with m.p. 163-165°. Recrystallization from dilute dioxan gave colorless needle crystals with m.p. 169-170°.

Found %: C 32.74, 32.87; H 2.30, 2.46. $C_{11}H_9O_3NHg$. Calculated %: C 32.71; H 2.24.

5-Phenylisoxazole mercuriacetate is readily soluble in dioxan and glacial acetic acid, and difficultly soluble in dichloroethane.

A solution of 36.5 g of 5-phenylisoxazole mercuriacetate in dioxan was treated with a solution of 10.75 g of potassium bromide in dioxan. The obtained precipitate was filtered and dried in vacuo over phosphorus pentoxide. We obtained 37.7 g (98%) of 5-phenylisoxazole mercuribromide with m.p. 230°, which was dissolved in 2 liters of dry dichloroethane. The obtained solution was treated with a solution of 14.2 g of bromine in 50 ml of dichloroethane, and the mixture boiled for 6 hours (until it became colorless). The dichloroethane was distilled off to dryness, and the bromo-5-phenylisoxazole was extracted from the residue with petroleum ether. Evaporation of the ether in vacuo gave 13 g (65%) of a yellow oil as residue, which crystallized completely on cooling. Vacuum-distillation gave an oil (b.p. 101-102° at 1 mm), which crystallized completely to colorless plates with m.p. 31-32°.

Found %: C 48.25, 48.28; H 2.75, 2.75. C_9H_6ONBr. Calculated %: C 48.24; H 2.69.

The mixed melting point with the bromo-5-phenylisoxazole, obtained by the direct bromination of 5-phenylisoxazole, was not depressed.

SUMMARY

1. The bromination or mercuration of 5-phenylisoxazole results in substitution only in the isoxazole ring. On nitration the substitution goes to the same degree in both the phenyl and isoxazole rings.

2. In substitution reactions of 5-phenylisoxazole the isoxazole ring is more active than the phenyl ring.

Received January 25, 1957

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*Original Russian pagination. See C. B. Translation.

REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

III. REACTION OF PHENOL WITH DIOLS IN THE PRESENCE OF PHOSPHORIC ACID

I. P. Losev and O. V. Smirnova

Continuing our investigations of the reaction of aromatic compounds with alcohols in the presence of acidic catalysts, we selected as one of our next problems a study of the reaction of phenol with diols. As study subjects we took the 1,4- and 1,3-butanediols.

Nothing could be found in the literature on the condensation of phenols with diatomic alcohols. The condensation was run by us under conditions similar to those used for the condensation of phenols with monoatomic alcohols in the presence of acidic catalysts.

The literature on the alkylation of phenols with alcohols and ethylenic hydrocarbons is quite extensive [1-17], indicating that various products of acidic character ($AlCl_3$, H_2SO_4, solution of concd. H_2SO_4 in acetic acid, BF_3, H_3PO_4, etc.) can be used as catalysts for the reaction. In most cases the alkylation goes with the formation of para-substituted phenols. For all practical purposes the ortho-substituted derivatives are not obtained, and only in isolated cases are they described as being the main reaction products.

We ran the condensation of phenol with diatomic alcohols, and specifically with diethylene glycol, 1,3-butanediol and 1,4-butanediol, in the presence of aluminum chloride and phosphoric acid. Positive results were obtained when phenol was condensed with 1,4-butanediol in the presence of phosphoric acid. Here we obtained two compounds – 4-(p-hydroxyphenyl)butanol (I) and 1,4-bis(p-hydroxyphenyl)butane (II).

$$p\text{-}HOC_6H_4CH_2CH_2CH_2CH_2OH$$

(I)

$$p\text{-}HOC_6H_4CH_2CH_2CH_2CH_2C_6H_4OH\text{-}p$$

(II)

EXPERIMENTAL

The condensation of phenol with diethylene glycol and with 1,3-butanediol in the presence of aluminum chloride and phosphoric acid leads to the formation of tarry products, soluble in benzene, alcohols, and other organic solvents. We were unable to isolate any individual organic compounds.

The condensation of phenol (40.0 g) and 1,4-butanediol (30.0 g) in the presence of phosphoric acid (166.6 g) with heating for 10 hours at 180-200° gave a mixture of products, which separated into two layers. The upper oily layer was separated from the lower acidic layer, washed until neutral, dried over calcium chloride, and vacuum-distilled at 2 mm. Six fractions were obtained from the distillation. The first two fractions represented products that were rich in the starting phenol.

Fraction 3 after redistillation gave a substance with b.p. 212-215°, corresponding to the monophenyl ether of 1,4-butanediol with d^{20}_4 1.0334, $n^{20}D$ 1.5350, MR_D 85.77; calc. 85.84.

Fraction 4 after redistillation proved to be 4-(p-hydroxyphenyl)-butanol (I):

B. p. 232-235°, d^{20}_4 1.0352, $n^{20}D$ 1.5301, MR_D 84.5; calc. 85.0.

Found %: C 72.71, 72.83; H 8.08, 8.32. M 167.5. $C_{10}H_{14}O_2$. Calculated %: C 72.30; H 8.41. M 166.0.

The obtained product (I) was acetylated with acetic anhydride under heating. To establish the structure of (I) we oxidized it (1.5 g, dissolved in 40.0 ml CH_3COOH) with a mixture composed of 43.0 g $K_2Cr_2O_7$, 2.3 g of glacial acetic acid and 4.3 ml of water for 1 hour at 60-70°. On conclusion of reaction the following fraction was isolated:

B. p. 221-223°, d^{20}_4 1.0482, $n^{20}D$ 1.5389.

Found %: C 73.80, 73.88; H 7.14, 7.21. M 160.0. $C_{10}H_{12}O_2$. Calculated %: C 73.20; H 7.29. M 164.0.

The analysis data indicate that the product obtained in the oxidation of (I) is the hydroxyphenylbutyraldehyde. The presence of the aldehyde group was shown by qualitative tests.

Fraction 5 after redistillation gave a substance with b.p. 247-249°, which corresponds to 1,4-bis(p-hydroxyphenyl)butane (II).

Found %: C 78.84, 79.11; H 7.41, 7.34. M 238. $C_{16}H_{18}O_2$. Calculated %: C 79.34; H 7.44. M 242.

SUMMARY

1. The reaction of diethylene glycol and 1,3-butanediol with phenol in the presence of $AlCl_3$ and H_3PO_4 leads to the formation of tarry products, soluble in most organic solvents.

2. The reaction of 1,4-butanediol with phenol in the presence of H_3PO_4 leads to the formation of 4-(p-hydroxyphenyl)butanol (I) and 1,4-bis(p-hydroxyphenyl)butane (II). The optimum conditions for running this reaction is to heat the reaction mixture at 200-220° in dilute phosphoric acid (d 1.5) medium, i.e., conditions that are more drastic than those indicated by various authors in the literature for running the condensation of phenol with monoatomic alcohols. Simultaneously with (I) and (II), tarry products are also obtained in this reaction, soluble in acetone and benzene [4, 8, 15].

Received December 10, 1956

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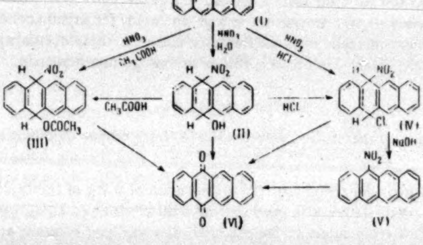
CHEMISTRY OF NAPHTHACENE

VII. NITRATION OF NAPHTHACENE*

N. P. Bedniagina, G. A. Panfilov and I. Ia. Postovskii

Due to the difficult availability of the hydrocarbon naphthacene, the chemistry of this compound has received comparatively little study up to now. Thus, for example, the nitration of naphthacene has not been reported in the literature. Our study of the reaction revealed that naphthacene on nitration behaves in the same manner as anthracene. Naphthacene gives unstable dihydronitro products due to the addition of nitric acid at the para-positions of one of the middle rings. Beginning at the second middle ring, addition does not proceed, apparently for the reason that addition at the first ring separates the molecule into two isolated aromatic systems – a benzene and a naphthalene system, neither having an active meso-position.

The nitration products of naphthacene, obtained in the present study, and their mutual transformations, are depicted in the scheme.



The first intermediate product in the nitration of naphthacene is 9-nitro-10-hydroxydihydronaphthacene (II). It is easily formed by treating naphthacene under cooling to 0-3° with nitric acid (d 1.36) or by reacting nitric acid at the same temperature with a suspension of naphthacene in glacial acetic acid. In the last case, as soon as a clear solution is obtained, it is poured into water, and here 9-nitro-10-hydroxydihydronaphthacene is obtained as a precipitate. If the reaction mass is not poured into water, but instead the stirring is continued, then the 9-nitro-10-hydroxydihydronaphthacene is easily acetylated, and soon yellow needles of 9-nitro-10-acetoxydihydronaphthacene (III) deposit from solution. The corresponding anthracene derivative is also known [1].

9-Nitro-10-chlorodihydronaphthacene (IV) was obtained in the same manner as the corresponding anthracene derivative [2] by treating a suspension of naphthacene in glacial acetic acid with nitric acid (d 1.36) at 0-3°, followed by the addition of concd. HCl to the obtained clear solution of 9-nitro-10-hydroxydihydronaphthacene. The chloro compound can also be obtained from 9-nitro-10-hydroxydihydronaphthacene if the latter is dissolved in glacial acetic acid and then treated with concd. HCl solution with cooling.

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* Communication VI: J. Gen. Chem. 20, 1711 (1950). (Original Russian pagination. See C. B. Translation.)

The obtained dihydronitro derivatives of naphthacene, the same as the corresponding products of the anthracene series, are quite unstable compounds. When heated in organic solvents, in an attempt to recrystallize them, they are easily and completely converted to pure p-naphthacenequinone. Here neither anaquinone nor other products could be found. This indicates that during nitration only addition at the para-positions took place.

Judging from the constants and the analysis data, the obtained dihydronitro derivatives represent quite pure compounds without further purification. The most stable 9-nitro-10-acetoxydihydronaphthacene can be recrystallized from glacial acetic acid heated to 50°.

The treatment of 9-nitro-10-chlorodihydronaphthacene with dilute alkali in the cold yields a red water-soluble substance, in all probability being the sodium salt of the acid form of the dihydronitro compound.* Probably, it is also possible to obtain other dihydronitro products in the naphthacene series, similar to those described for anthracene [4], for example, 9-nitro-10-methoxy-(ethoxy)-dihydro derivatives, etc.

We were able to obtain the most interesting nitro product of the naphthacene series, namely 9-nitronaphthacene (V), only from 9-nitro-10-chlorodihydronaphthacene (IV) by treating the latter with 30% sodium hydroxide solution at 50° for several hours. When the other dihydronitro compounds (II) and (III) were treated with either alkali solution, pyridine or alcoholic caustic solution, with slight heating, we were unable to obtain the nitronaphthacene, and instead p-naphthacenequinone (VI) was obtained in all cases. It is possible that under certain conditions these transformations take place, as is the case in the anthracene series [5].

The preparation and study of 9-nitronaphthacene was complicated by its extreme instability. It is much less stable than 9-nitroanthracene, and when heated in various organic solvents, or when the solutions are allowed to stand in the cold, especially in the light, it suffers rapid decomposition and is converted to p-naphthacenequinone. 9-Nitronaphthacene can be recrystallized if it is added to boiling glacial acetic acid, and after filtering, the solution is cooled rapidly. In the dry crystalline state it is stable and can be stored. In contrast to the yellow 9--nitroanthracene, 9-nitronaphthacene has a red color.

The color of the obtained products with concd. H_2SO_4 and their fluoroescence under an ultraviolet lamp can serve as a rapid qualitative test for their identification. All of the derivatives containing a nitro group give a deep blue coloration with concd. H_2SO_4, in contrast to a green color for naphthacene, and a red color for p--naphthacenequinone. 9-Nitronaphthacene does not fluoresce under an ultraviolet lamp, in contrast to all of the other compounds described here, which give either a yellow or orange luminescence.

EXPERIMENTAL

Naphthacene was obtained by the method described in [5] from ethyne diphthalide by distillation with zinc dust.

9-Nitro-10-hydroxydihydronaphthacene (II). To a suspension of 0.2 g of finely divided napthacene in 4 ml of glacial acetic acid was gradually added with good stirring 4 ml of HNO_3 (d 1.36), previously freed of nitrogen oxides by blowing with air. This temperature of the reaction mass was kept constant at 0-3°. After stirring for 20-25 minutes the suspension was converted to a clear solution, which was poured into cold water. The resulting light-yellow microcrystalline precipitate was filtered, repeatedly washed with water, and dried in a vacuum-desiccator over $CaCl_2$. Yield 0.21 g (quantitative). M.p. 90-95°.

Found %: N 4.92. Active H 1.2. $C_{18}H_{13}O_3N$. Calculated %: N 4.79. Active H 1.0.

The compound is readily soluble in alcohol, benzene, acetic acid and dioxan but when recrystallized from a hot solvent it is quantitatively converted to p-naphthacenequinone, obtained as long slender yellow needles with m.p. 285-290°. If the compound is dissolved in dioxan at room temperature, followed by evaporation of the solvent in vacuo, then it becomes possible to obtain 9-nitro-10-hydroxydihydronaphthacene as coarse transparent prisms. M.p. 90-95°.

9-Nitro-10-hydroxydihydronaphthacene can also be obtained if naphthacene is nitrated in the absence of a solvent: 0.2 g of powdered naphthacene was stirred at 0-5° for several hours with 20-25 ml of HNO_3 (d 1.36). The suspension gradually changed from an orange to a light-yellow color. The microcrystalline precipitate was filtered, washed with water, and dried in vacuo at room temperature. M.p. 90-95°, and not depressing the melting point when mixed with the compound described above.

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* A similar salt was described in the anthracene series [3].

9-Nitro-10-acetoxydihydronaphthacene (III). This compound was obtained under conditions similar to the preceding experiment, but here the obtained clear reaction mass was not poured into water, but instead it was allowed to stand at 0-5°. The yellow needles or prisms that deposited in approximately an hour were filtered, washed with water, and air-dried. Yield 0.22 g (quantitative). M.p. 270-275°. Considerably less soluble in the cold in acetic acid, alcohol, and other solvents, than the hydroxy derivative (II). When recrystallized from hot solvents it also suffers quantitative conversion to p-naphthacenequinone. We found that the crude product could be recrystallized from acetic acid, heated to 50-60°.

Found (for the unrecrystallized product) %: N 4.55. $C_{20}H_{15}O_4N$. Calculated %: N 4.20.

9-Nitro-10-acetoxydihydronaphthacene can also be obtained from the hydroxy compound (II). 9-Nitro-10-hydroxydihydronaphthacene (0.1 g) was dissolved with cooling in 4-5 ml of glacial acetic acid. The solution on standing soon began to deposit crystals of the acetyl derivative (III). M.p. 270-275°, not depressing the melting point when mixed with the compound obtained above.

9-Nitro-10-chlorodihydronaphthacene (IV). Pulverized naphthacene (0.2 g) was suspended in 4 ml of glacial acetic acid and 4 ml of HNO_3 (d 1.36) was added with cooling to 0-3°. As soon as the suspension had changed to a clear solution a mixture of 4 ml of hydrochloric acid (d 1.19) and 2 ml of glacial acetic acid was added, and the reaction mass was stirred for 1 hour at a temperature not exceeding 5°. The yellow finely crystalline precipitate (needles) was filtered, washed with 2-3 ml of acetic acid, and then well with water. Yield 0.21 g. M.p. 130-135° (with decompn.).

Found %: N 4.69, 4.60. $C_{18}H_{12}O_2NCl$. Calculated %: N 4.51.

The chlorine content was 1-2% less than the calculated (9-10% instead of 11.48%). Evidently the product contains the hydroxy and acetoxy compounds (II and III) as impurities. It proved that we could not recrystallize the compound, since when heated in solvents it is quantitatively converted to p-naphthacenequinone, while if it is dissolved in benzene, dioxan or chloroform in the cold, followed by evaporation of the solvent, a viscous mass is obtained.

9-Nitro-10-chlorodihydronaphthacene can also be obtained from the hydroxy product (II) if the latter is dissolved in glacial acetic acid, and the solution treated with concentrated hydrochloric acid at 3-5°.

9-Nitronaphthacene (V). The moist freshly prepared 9-nitro-10-chlorodihydronaphthacene (IV), obtained from 0.2 g of naphthacene, was rubbed in a small dish with 4 ml of 30% NaOH, with heating to 50° on the water bath. The slurry of crystals gradually assumed a red color. After 2 hours the reaction mass was diluted with water and the precipitate filtered, washed well with water, and dried in a vacuum-desiccator. Yield 0.17-0.18 g. Red microcrystalline powder, m.p. 190-192° (with decompn.).

Found %: N 5.00. $C_{18}H_{11}O_2N$. Calculated %: N 5.12.

9-Nitronaphthacene can be recrystallized from acetic acid. For this the moist freshly obtained 9-nitronaphthacene is dissolved in glacial acetic acid (5-6 ml per 0.2 g), previously heated to the boil, and the hot solution is rapidly filtered and cooled; clusters of brick-red needles deposit. M.p. 190-192°. But if the acetic acid solution is boiled for only a few minutes, then the pure p-naphthacenequinone is obtained as long yellow needles, m.p. 285-290°.

SUMMARY

1. It was established that the nitration of naphthacene gives the addition product — 9-nitro-10-hydroxydihydronaphthacene (II), which when reacted with acetic acid is converted to 9-nitro-10-acetoxydihydronaphthacene (III), and when reacted with concentrated hydrochloric acid is transformed to 9-nitro-10-chlorodihydronaphthacene (IV).

2. 9-Nitronaphthacene (V) was obtained by the action of 30% NaOH on 9-nitro-10-chlorodihydronaphthacene (IV).

3. It was established that the dihydronitro derivatives of naphthacene (II-IV) and 9-nitronaphthacene are even less stable than the corresponding compounds of the anthracene series, and are easily converted when heated

in solvents or without a solvent to p-naphthacenequinone.

Received January 7, 1957

Ural Polytechnic Institute

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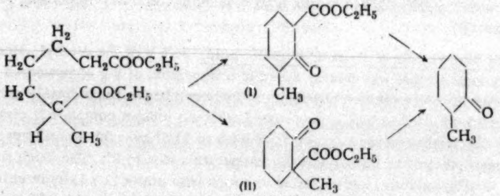
*Original Russian pagination. See C. B. Translation.

INVESTIGATION IN THE FIELD OF THE DIECKMANN REACTION

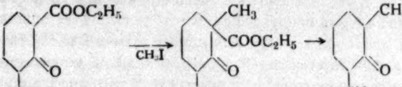
III. CYCLIZATION OF THE DIETHYL ESTER OF α-METHYLPIMELIC ACID

N. S. Vul'fson and V. I. Zaretskii

Dieckmann [1] described the cyclization of the diethyl ester of α-methylpimelic acid and considered that this reaction gave 2-methyl-6-carbethoxycyclohexanone, which, however, was not isolated in a pure form. The author proposed a structure for the product obtained on the basis of a qualitative reaction with ferric chloride, the preparation of a copper salt and the conversion to 2-methylcyclohexanone by hydrolysis and decarboxylation. However, as the scheme shows, the formation of 2-methylcyclohexanone from the diethyl ester of α-methylpimelic acid may proceed by two paths and, consequently, the formation of 2-methylcyclohexanone cannot be considered as proof of the structure of the cyclic β-ketoester formed as an intermediate.



In continuing the study of the mechanism of cyclization of esters of unsymmetrical dicarboxylic acids by Dieckmann's method [2], we set out to establish more accurately the structure of the cyclic β-ketoester, formed during the cyclization of the diethyl ester of the α-methylpimelic acid. The only cyclization product was β-ketoester (I). We could not detect the formation of β-ketoester (II). With an aqueous ferric chloride solution the cyclization product gave a violet-red color and had constants different from those of 2-methyl-2-carbethoxycyclohexanone, which we obtained during the synthesis of the diethyl ester of α-methylpimelic acid. The structure of the cyclization product was confirmed by its methylation and subsequent decarboxylation of the 2,6-dimethyl-6-carbethoxycyclohexanone obtained to 2,6-dimethylcyclohexanone, described previously by Ruzicka [3].



2-Methyl-2-carbethoxycyclohexanone (II) should not be methylated under similar conditions and this was confirmed experimentally. The unusual formation of the β-ketoester (I) in the cyclization of the diethyl ester α-methylpimelic acid is, apparently, explained by the increase in electron density at the α-carbon atom due to the I-effect of the CH_3 group, which hinders proton dissociation and the formation of the organic anion, necessary for cyclization.

EXPERIMENTAL

2-Carbethoxycyclohexanone was prepared by the method of Schneider, Brooks and Shapiro [4]; after redistillation the material had b.p. 77-83° at 2 mm, $n^{20}D$ 1.4810.

2-Methyl-2-carbethoxycyclohexanone was prepared by a slightly modified method [5].

To a mixture of 103.5 g of 2-carbethoxycyclohexanone and 50 ml of methyl iodide, cooled to −15°, a solution of sodium methylate (from 15.1 g of sodium and 183 ml of methanol) was added over a period of 15 minutes at −13° to −10°. The mass gradually thickened but when the temperature was raised to 0°, it became liquid again. The mass was stirred for 3 hours at −5° and left overnight at −5° (in a refrigerator). The excess methyl iodide (~19.5 g) and part of the methanol was distilled off on a boiling water bath; the total volume of the distillate was 70 ml. The cooled residue was treated with 700 ml of water, shaken in a separating funnel and extracted with ether (5 × 150 ml). The ether solution was washed with 15% potassium hydroxide solution in 75-ml portions until it gave a negative reaction with an aqueous solution of ferric chloride, washed with water until the wash water gave a neutral reaction with brilliant yellow paper and then dried over anhydrous sodium sulfate. The solvent was distilled off and the residue distilled in vacuum. The yield of 2-methyl-2-carbethoxycyclohexanone was 96.4 g (86%) and the product had b.p. 80-81° at 2.5 mm, $n^{20}D$ 1.4540, d^{20}_4 1.044. It did not give a color reaction with ferric chloride solution. According to literature data the b.p. is 113-114° at 10-11 mm [5], 100-104° at 9 mm[6].

Diethyl ester of α-methylpimelic acid [7]. To a solution of sodium ethylate (from 2.2 g of sodium and 100 ml of anhydrous alcohol) was added 92 g of 2-methyl-2-carbethoxycyclohexanone, the mixture boiled for 6 hours and then cooled, 400 ml of water added, the mixture acidified to pH ~ 6.5 with acetic acid and the product extracted with ether (200 + 100 ml) and dried over anhydrous sodium sulfate. The solvent was distilled off and the residue distilled in vacuum to give a fraction boiling at 110.5-118° at 3.5 mm, which was redistilled to give 81 g (70%) of the ester with b.p. 115-118° at 4 mm, $n^{20}D$ 1.4318, d^{20}_4 0.9823. According to the literature data it has b.p. 140° at 12 mm [8].

Cyclization of the diethyl ester of α-methylpimelic acid. 34.5 g of the diethyl ester of α-methylpimelic acid and 0.3 ml of anhydrous alcohol was quickly added to a suspension of 5 g of powdered sodium in 125 ml of benzene (dried over sodium). The evolution of bubbles of hydrogen began immediately and the mass warmed up very slowly. It was carefully heated to boiling and stirred until the sodium completely disappeared (~ 3 hours). The temperature of the vigorously boiling mass fell from 81.5 to 77.5° over 30-40 minutes. The mass was cooled to −7°, when a voluminous precipitate formed and the temperature rose to 3°. The thick suspension was poured onto 100 g of ice (in a cooling mixture) and acidified to congo with dilute (1 : 1) hydrochloric acid, the benzene layer separated, the aqueous layer extracted with 50 ml of benzene and the combined benzene solution washed successively with 5% soda solution (40 ml) and water (50-ml portions) until neutral to brilliant yellow paper. The washed solution was dried with anhydrous sodium sulfate, the solvent distilled off and the residue distilled in vacuum to give 2-methyl-6-carbethoxycyclohexanone (I); the yield was 19.4 g (70%), the b.p. 84.5-86° at 2.5 mm, $n^{20}D$ 1.4720, d^{20}_4 1.0455; with an aqueous solution of ferric chloride the product immediately gave a violet red color; MR_D 49.32; calculated for the enol 48.89, for the ketone 47.85. According to literature data: b.p. 97° at 4 mm [9].

Found %: C 64.81; H 8.87. $C_{10}H_{16}O_3$. Calculated %: C 65.22; H 8.69.

2,6-Dimethyl-6-carbethoxycyclohexanone. Over a period of 10 minutes, a solution of sodium methylate (from 1.35 g of sodium and 16 ml of dry methanol) was added dropwise to a stirred mixture of 10 g of 2-methyl-6-carbethoxycyclohexanone and 4.6 g of methyl iodide at −10° to −7°. Five minutes after the end of the addition, the mass thickened at −6° and it was kept at a temperature of from 0 to −3° for 4 hours and then overnight at 4-5°. The solvent was distilled off in vacuum (58-60 mm) with a bath temperature of 50°, 100 ml of water added to the cooled residue, which was extracted with ether (4 × 25 ml), and the ether solution washed several times with 20-ml portions of 15% potassium hydroxide solution until it gave a negative qualitative reaction with an aqueous solution of ferric chloride and then with water (25-ml portions) until neutral to brilliant yellow paper. The solution was dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled to give 2,6-dimethyl-6-carbethoxycyclohexanone; the yield was 8.2 g (76.8%), the b.p. 79-85° at 2.5 mm, $n^{20}D$ 1.4528; the product did not give a color with ferric chloride. According to the literature data: b.p. 112-118° at 12 mm [6].

Found %: C 66.84; H 9.05. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.09.

2,6-Dimethylcyclohexanone [3]. 7.7 g of potassium hydroxide was dissolved with boiling in 11.5 ml of anhydrous methanol, the hot solution quickly cooled to −8°, 9 g of 2,6-dimethyl-6-carbethoxycyclohexanone added in one portion to the thick mass, which was externally cooled in a mixture of ice and salt, and the mixture shaken and left at room temperature for 9 days. Part of the solvent was distilled off in vacuum (~ 60 mm) with a bath temperature of ~25°, 50 ml of water added to the residue, the mass shaken, the oil which separated dissolved in 50 ml of ether and the aqueous layer extracted with ether (2 × 50 ml). The aqueous layer was acidified with concentrated hydrochloric acid until strongly acid to congo and boiled for 10 hours, the very small amount of oil which separated extracted with ether and the extract added to the main ether solution. The combined ether solution was washed with water and dried over anhydrous sodium sulfate. The solvent was distilled off and the residue vacuum distilled to give 2,6-dimethylcyclohexanone; the yield was 2.5 g (44%), the b.p. 61-61.5° at 12-13 mm, $n^{20}D$ 1.4465. According to literature data, b.p. 62° at 12 mm, $n^{20}D$ 1.4481 [5].

Found %: C 76.44; H 11.20. $C_8H_{14}O$. Calculated %: C 76.19; H 11.11.

The semicarbazone had m.p. 176-177°; according to literature data: m.p. 176° [3].

Found %: C 59.01; H 9.33. $C_9H_{17}ON_3$. Calculated %: C 59.03; H 9.29.

Attempted methylation of 2-methyl-2-carbethoxycyclohexanone. 28 g of 2-methyl-2-carbethoxycyclohexanone was treated with methyl iodide as in the case of 2-methyl-6-carbethoxycyclohexanone and we obtained 19.2 g of material with b.p. 78.5-85° at 2 mm, $n^{20}D$ 1.4555-1.4570.

2-Methylcyclohexanone. 8.4 g of the methylation product obtained above was boiled for 20 hours with 100 g of ~20% sulfuric acid. The reaction mixture was extracted with ether (3 × 50 ml) and the ether solution washed with water, dried and distilled. We obtained 2-methylcyclohexanone with b.p. 160-164° at 740 mm, $n^{20}D$ 1.4480, d^{20}_4 0.9217. According to literature data: b.p. 166°, $n^{20}D$ 1.4483 [10]; $n^{20}D$ 1.4475 [11], d^{20}_4 0.9231 [12]. The semicarbazone had m.p. 191-192° (from alcohol). It did not depress the melting point of 2-methylcyclohexanone semicarbazone. According to literature data 2-methylcyclohexanone semicarbazone has m.p. 191° [10, 13].

SUMMARY

Cyclization of the diethyl ester of α-methylpimelic acid by Dieckmann's method was studied. It was shown that 2-methyl-6-carbethoxycyclohexanone was the primary reaction product; the formation of 2-methyl-2-carbethoxycyclohexanone was not observed. The structure of 2-methyl-6-carbethoxycyclohexanone was confirmed by preparing 2,6-dimethylcyclohexanone by methylation with methyl iodide, followed by hydrolysis and decarboxylation.

Received January 21, 1957

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Intermediates and Dyes

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CATALYTIC CONVERSIONS OF HALOGEN DERIVATIVES OF THE AROMATIC SERIES

IV. A STUDY OF THE MECHANISM OF THE CATALYTIC ISOMERIZATION OF MONOCHLORONAPHTHALENES USING LABELED ATOMS

N. N. Vorozhtsov, jr. and V. A. Koptiug

In studying monobromonaphthalene isomerization in the presence of ferric chloride, Dutch investigators [1] assumed that this reaction was due to the reversibility of the bromination process both in liquid phase and vapor phase isomerization.

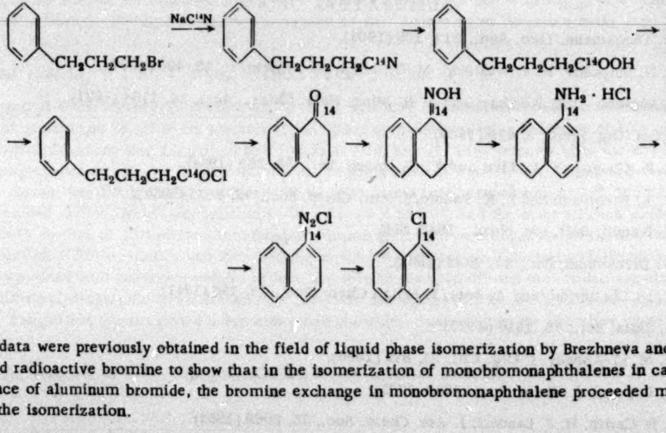
$$\alpha\text{-}C_{10}H_7Br + HBr \rightleftarrows C_{10}H_8 + Br_2 \rightleftarrows \beta\text{-}C_{10}H_7Br + HBr$$

Under these conditions isomerization was actually accompanied by the formation of naphthalene and dibromonaphthalenes.

However, in work devoted to the study of vapor phase catalytic isomerization of monochloro- and monobromonaphthalenes over aluminum oxide and aluminosilicate, one of us et al. [2, 3] obtained data which seemed to indicate an intermolecular course for the reaction.*

This work shows that in the isomerization of 1-chloronaphthalene-1-C^{14} on an aluminosilicate catalyst at 355-365°, mainly 2-chloronaphthalene-1-C^{14} is formed. This result excluded the possibility of the intermediate formation of naphthalene, as in this case isomerization of 1-chloronaphthalene-1-C^{14} would give an equimolecular mixture of 2-chloronaphthalenes, labeled in positions 1, 4, 5 and 8.

The 1-chloronaphthalene-1-C^{14}, which has not been described previously, was synthesized by the scheme



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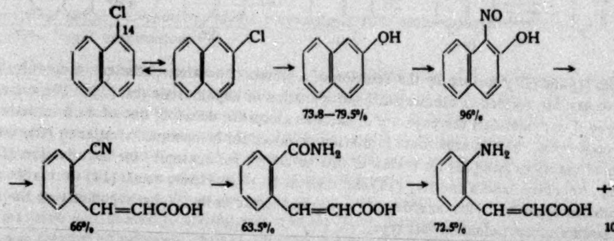
* Analogous data were previously obtained in the field of liquid phase isomerization by Brezhneva and Roginskii [30] who used radioactive bromine to show that in the isomerization of monobromonaphthalenes in carbon disulfide in the presence of aluminum bromide, the bromine exchange in monobromonaphthalene proceeded much more slowly than the isomerization.

γ-Phenylpropyl bromide and sodium cyanide gave γ-phenylbutyric acid, labeled with radiocarbon in the carboxyl group, and this was converted by Johnson and Glenn's method [4] to 1-keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} (α-tetralone-1-C^{14}), which was isolated as the oxime in 92.8% yield (calculated on the initial cyanide).

To convert the 1-keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} oxime to 1-naphthylamine-1-C^{14} we used the reaction described by Schroeter [5], which proceeds on heating the oxime with acetic anhydride in glacial acetic acid in a current of hydrogen chloride. This reaction, carried out by a method we developed,[*] gave a 51.8% yield of 1-naphthylamine-1-C^{14} hydrochloride. A mixture of α- and β-naphthols (16.8% yield) was isolated as a side product.

1-Chloronaphthalene-1-C^{14} was prepared in ~50% yield from 1-naphthylamine-1-C^{14} hydrochloride by Sandmeyer's reaction [6, 7].

1-Chloronaphthalene-1-C^{14} was isomerized on an aluminosilicate catalyst in a current of hydrogen chloride at 355-365°. The 2-chloronaphthalene thus formed was degraded to split out the carbon atom in position 1, by the scheme



2-Chloronaphthalene was treated with 0.8 N sodium hydroxide solution at 365° to give 2-naphthol and nitrosation of the latter [8] gave 1-nitroso-2-naphthol.

The C_1-C_2 bond of the naphthalene nucleus was split by rearranging 1-nitroso-2-naphthol into cis-o-cyanocinnamic acid (Beckmann rearrangement of the 2nd type), by treatment with p-toluenesulfonyl chloride in an alkaline medium [9]. Boiling the cis-o-cyanocinnamic acid obtained with dilute hydrochloric acid gave trans-o-carbamidocinnamic acid [10], which was degraded by the Hofmann reaction (treatment with sodium hydrobromite) to give trans-o-aminocinnamic acid and carbon dioxide. The latter contained the carbon from position 1 in the 2-chloronaphthalene molecule.

The results of measuring the radioactivity of trans-o-carbamidocinnamic and trans-o-aminocinnamic acids and the carbon dioxide are given in the table.

Compound	Radioactivity	
	μC/ mole	%
o-$C_6H_4(CONH_2)CH=CHCOOH$	2006 ± 19	100
o-$C_6H_4(NH_2)CH=CHCOOH$	125 ± 0.5	6.2
CO_2	1855	92.5

Thus, 93.8% of the 2-isomer formed during 1-chloronaphthalene-1-C^{14} isomerization consisted of 2-chloronaphthalene-1-C^{14} and this indicated that at least 91.7%[**] of the 1-chloronaphthalene molecules were isomerized to 2-chloronaphthalene without the intermediate formation of naphthalene.

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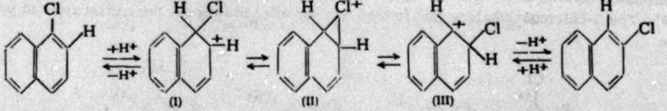
[*] The work on the mechanism of this reaction will be described in another paper.

[**] $(100 - \frac{6.2}{3} \cdot 4) = 91.7.$

The retention of 6.2% of the radioactivity by trans-o-aminocinnamic acid may be due to two reasons: partial isomerization by an intermolecular mechanism or the presence of some rearrangement during the preparation of 1-chloronaphthalene-1-C^{14}, which resulted in the formation of 1-chloronaphthalene with the radiocarbon in a different position.

The first hypothesis is supported by the fact that isomerization of monochloronaphthalenes at 550° gave 29.4% of naphthalene [3]. Therefore, it is possible that the retention of 6.2% of activity by trans-o-aminocinnamic acid is due to partial (8.3%) isomerization at 355-365° by an intermolecular mechanism. However, this cannot yet be confirmed with the available data.

The reversible transfer of the halogen during the isomerization of monohalonaphthalenes from position 1 to position 2 may be represented by the following mechanism.

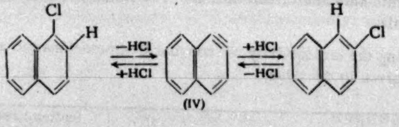


The carbonium ions (I) and (III), formed by the addition of a proton to a halonaphthalene molecule, are analogous to the intermediate cations, formed in electrophilic halogenation of naphthalene (cf. [1]). The conversion (I) $\rightleftharpoons$(III) is readily understood if one considers the capacity of halogen atoms for donating one of their unshared electron pairs to form a second bond. The intermediate formation of halonium compounds, similar to (II), was postulated earlier for a series of reactions (see [11] for review of this problem), for example, for the addition of halogen at a double bond [12]. Recently Sandin and Hay [13] and then A. N. Nesmeianov et al. [14] were able to prepare bromonium and chloronium salts. This considerably strengthened the basis for the hypothesis on the formation of intermediate compounds of the halonium salt type.

Fluoronium compounds have not been obtained up to now. This is apparently the result of the high ionization potential of fluorine as compared with that of carbon (ionization potentials in volts: C 11.2, Br 11.8, Cl 13.0, F 18.6) and explains the absence of isomerization in the case of monofluoronaphthalenes [3].

The need for a proton for isomerization to proceed explains why halonaphthalenes isomerize especially smoothly in the presence of hydrogen halides (without them, the catalyst provides the protons).

Another possible mechanism is the following



Huisgen [15] assumed the intermediate formation of (IV) in order to explain the fact that phenyllithium treatment of both 1- and 2-fluoronaphthalene followed by carboxylation gave a mixture of 1-phenyl-2-carboxylic and 2-phenyl-1-carboxylic acids of naphthalene of the same composition. Witting [16] and Roberts [17] confirmed this assumption by proving the intermediate formation in a series of reactions of cyclohexadienyne, of which (IV) is an analog.

The intermediate formation of (IV) was also accepted as a working hypothesis [18] to explain the isomeric conversions of naphthalene derivatives and, in particular, to explain the isomerization of deuteronaphthalenes when their vapor was passed over silica gel.

It should be noted, however, that the intermediate formation of a compound of type (IV) is characteristic of reactions proceeding under conditions when there is the possibility of the formation of a carbanion as a result of the elimination of the hydrogen atom, situated in the position ortho to the halogen, as a proton [16, 17]. This occurs, for example, under the effect of such strong bases as an NR$_2^-$ ion.

However, in our case of chloronaphthalene isomerization on an acid catalyst in the presence of hydrogen chloride (as in the case of deuteronaphthalene isomerization on silica gel [18]) such conditions for carbanion formation do not exist, which makes the mechanism with the intermediate formation of (IV) questionable.

Such a mechanism for halonaphthalene isomerization is also contrary to the fact that isomerization of chloro- and bromonaphthalenes in the presence of hydrogen fluoride does not give fluoronaphthalenes [3].

From these considerations it appears to us that the mechanism providing for the intermediate formation of halonium salts in the isomerization of halonaphthalenes is better substantiated.

The exchange of halogen in the reaction of halonaphthalenes with hydrogen halides, observed in previous work [3], should be considered not as a result of isomerization, but as a parallel process. This was confirmed by the fact that under conditions when fluoronaphthalenes were not isomerized, fluorine was, all the same, substituted by chlorine [3].

EXPERIMENTAL

Measurement of the radioactivity of the preparations. The preparations were converted into barium carbonate using a Van Slyke "wet" combustion.

Into flask 1 of the apparatus illustrated in Fig. 1 (a modified form of the apparatus of Lindenbaum et al. [19]) was placed a sample of the substance containing 8-9 mg of carbon, in a quartz boat, and 1.1 g of a mixture of potassium iodate and potassium dichromate (2 : 1). 15 ml of ~0.2 N barium hydroxide solution, containing 20 g of barium chloride per liter, was placed in trap 2 and the system evacuated through taps 3 and 4 to a residual pressure of 20 mm. Taps 3 and 5 were closed, the stopper with tap 4 was removed and the funnel 6 charged with 10 ml of a mixture of 20% oleum (chemically pure) and 88% phosphoric acid [20], after which the funnel was closed with a tube filled with ascarite. Almost the whole of the liquid mixture was released through tap 5 into flask 1, whose contents were then heated to boiling with a small flame, boiling was continued for 10 minutes and then the mixture was left for 30 minutes. During this time the suspension of barium carbonate in trap 2 rose up the bubbler tube. This was prevented by carefully admitting air through tap 5. Then the suspension of barium carbonate was quickly transfered to a titration flask (CO_2-free water was used for rinsing) and the excess barium hydroxide titrated with 0.1 N hydrochloric acid in the presence of phenolphthalein. The carbon content of the substance was calculated from the hydrochloric acid consumed (control on completeness of combustion).

For the preparation of samples for radioactivity measurement from the barium carbonate suspension, we used the method described in [21], with the only difference that the guard ring underneath also had a flange, which covered irregularities in the edges of the sample. With a sample surface of 5.02 cm^2 (diameter 25.3 mm), the uncovered part amounted to 3.80 cm^2 (diameter 22.0 mm). The suspension of barium carbonate was kept for 12 hours at room temperature before filtration.

The activity of the sample was measured on apparatus B with an end window counter with a mica window thickness of 1.3 mg/cm^2 and a resolving time of $2.2 \cdot 10^{-4}$ sec and the separation between the sample surface and the window was 15 mm.

In all cases the samples were "infinitely" thick, i.e., thicker than 25 mg/cm^2. The counting time for the samples was chosen so that the relative mean square error of measurement was not greater than 1%.

The count rate found was corrected for background, the resolving capacity of the counter and its counting efficiency. From the corrected count rate (R_{∞}), we calculated the absolute molar activity from a slightly modified form of Vasil'ev's formula [21]

$$A = 197000 \frac{1.46 C_E \cdot b \cdot R_{\infty}}{S} \cdot n\mu C/\text{mole},$$

where n is the number of carbon atoms in a molecule of the given compound. The coefficient C_E for our apparatus equalled $4.25 \cdot 10^{-6}$ μC·min/count.

γ-Phenylpropyl bromide. A mixture of 200 g of γ-phenylpropyl alcohol ($n^{20}D$ 1.5245), 600 g of 40% hydrobromic acid and 295 g of 96% sulfuric acid was boiled for 14 hours; the reaction product was steam distilled, washed with concentrated sulfuric acid, soda solution and water, dried with calcium chloride and distilled in vacuum. The yield of γ-phenylpropyl bromide was 259 g (88.7%) and the material had b.p. 109° (12 mm), $n^{20}D$ 1.5445.

γ-Phenylbutyric acid labeled with C^{14}. A solution of 24.0 g (120.4 mmoles) of γ-phenylpropyl bromide, 0.08 g (1.6 mmoles) of radioactive sodium cyanide (activity ~1.3 mC) and 5.20 g of 85.5%* sodium cyanide (90.6 mmoles of 100% cyanide) in 140 ml of ethyl alcohol and 20 ml of water was heated in a flask with a ground joint condenser on a glycerol bath at 100° (bath temperature) for 27.5 hours. To the solution of γ-phenylbutyronitrile obtained was added a solution of 20.6 g (367 mmoles) of potassium hydroxide in 40 ml of ethyl alcohol and 20 ml of water and the solution heated at 100° for a further 30 hours. Then 170 ml of alcohol was distilled off, 50 ml of water added and the neutral substances steam distilled off. The solution left in the flask was filtered into the flask of a continuous extractor [23], acidified with 45 ml of hydrochloric acid (d 1.172; 410 mmoles) and extracted with benzene (125 ml) for 13 hours. The γ-phenylbutyric acid was isolated from the dried benzene solution by evaporation in vacuum at a bath temperature of 50-60°

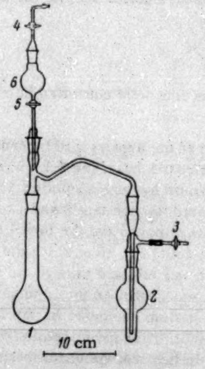


Fig. 1. Apparatus for combustion of materials (according to Van Slyke).
1) Combustion flask; 2) trap with barium hydroxide solution; 3, 4, 5) taps; 6) dropping funnel.

1-Keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} and its oxime. 21.5 g (103 mmoles) of phosphorus pentachloride was added in small portions to the impure γ-phenylbutyric acid. When the evolution of hydrogen chloride ceased, the mixture was heated to 50° (bath temperature) and kept at that temperature for 5 minutes; 10 ml of anhydrous, thiophene-free benzene was added and a mixture of benzene and volatile phosphorous compounds was distilled off in vacuum at a bath temperature of 60-70°. The addition and distillation of the benzene was repeated 4 more times.

The γ-phenylbutyryl chloride obtained was dissolved in 24 ml of anhydrous benzene and after 25 minutes added to a suspension of 17.5 g (131 mmoles) of anhydrous aluminum chloride in 60 ml of anhydrous, thiophene-free benzene, which was stirredand cooled. The temperature of the reaction mixture was kept below 10°. After the addition of the acid chloride, the reaction mixture was stirred for 35 minutes at 6-10°, then in 30 minutes the temperature was raised to 22° and kept there for 3 hours and the reaction mixture left overnight.

With stirring, 100 ml of dilute hydrochloric acid (1 : 1) (the temperature of the mixture was kept below 15°) was added to the mixture obtained and the mass kept at 10° for 30 minutes. The two-layer solution was filtered off, the organic layer separated and the aqueous layer extracted three times with ether. The organic layer was washed with sodium bicarbonate solution and water, dried with potassium carbonate and the solvent distilled off in vacuum.

The α-tetralone-1-C^{14} obtained, 12.7 g (183 mmoles) of hydroxylamine hydrochloride and 12.8 g (92.5 mmoles) of potassium carbonate were dissolved with heating in 100 ml of methyl alcohol and 45 ml of water and the solution boiled for 45 minutes. Activated charcoal (~ 0.5 g) was added to the solution, which was heated for a further 10 minutes and filtered through a heated funnel. The filter was washed with 50 ml of boiling methyl alcohol. When the methanol solution was cooled, the α-tetralone-1-C^{14} oxime crystallized out. For a more complete separation, the solution was diluted with 150 ml of water (50 ml every 24 hours) before removal of the oxime. The yield of α-tetralone-1-C^{14} oxime with m.p. 98-100° was 12.77 g. According to literature data, α-tetralone oxime has m.p. 103° [24]. Evaporation of the methyl alcohol from the mother liquor yielded an additional amount of oxime, which was purified by recrystallization from aqueous methyl alcohol. The yield was 1.05 g and the m.p. 92-95°.

The total yield of α-tetralone-1-C^{14} oxime was 92.8% (on the initial cyanide).

1-Naphthylamine-1-C^{14} hydrochloride. 10.5 ml (111 mmoles) of acetic anhydride was added to a solution of 13.65 g (84.7 mmoles) of α-tetralone-1-C^{14} oxime in 86 ml of 99.8% acetic acid (solidification point 16.3°), prepared in a flask fitted with a reflux condenser and a bubbler tube. After 1-1.5 minutes the whole mixture thickened due to the liberation of crystals of the acetyl derivative of the oxime. When the temperature of the bath was raised to 100° over 2 hours, the acetyl derivative of the oxime dissolved, giving a solution which gradually acquired a red violet color. The reaction mixture was kept for 2.5 hours with the bath temperature at 102-108°, while a stream of dry hydrogen chloride was passed through the bubbler. During this time, crystals of 1-naphthylamine-1-C^{14} hydrochloride separated from the solution. (Crystals of the hydrochloride periodically stopped up the bubbler tube; to remove the "plug" formed, we used a glass rod set in a rubber seal in the bubbler tube.) A condenser with a Claisen head was connected to the flask and the acetic acid carefully distilled off from the suspension obtained in vacuum (bath temperature 80°). The residue was treated with 120 ml of hydrochloric acid (1 : 1), heated on a bath to 140-145° (the crystalline precipitate then dissolved) and kept at this temperature for 7.5 hours. On cooling, the solution, whose surface was covered with a small layer of a viscous oil, deposited a yellowish crystalline precipitate of 1-naphthylamine-1-C^{14} hydrochloride.

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* The analysis was carried out by Liebig's method [22].

To remove tarry materials from the hydrochloride, the mixture obtained was shaken with 60 ml of chloroform for several minutes. After this, the 1-naphthylamine-1-C^{14} hydrochloride was filtered off, washed three times with 15-ml portions of chloroform and dried in vacuum over calcium chloride. The slightly grey, crystalline product was obtained in a yield of 7.60 g (49.8%). Analysis by diazotization of samples, obtained in model experiments, showed that 1-naphthylamine hydrochloride content of similar preparations was 95-98%.

After separation of the chloroform, the aqueous layer was washed with benzene and then extracted with ether after being made alkaline with a 20% solution of sodium hydroxide. The ether extract was dried over potassium hydroxide and then treated with dry hydrogen chloride to give a further 0.30 g (2.0%) of 1-naphthylamine-1-C^{14} hydrochloride.

Extraction of the red-brown chloroform layer with 10% sodium hydroxide solution yielded 2.06 g (16.8%) of a mixture of 1- and 2-naphthols with m.p. 106-109°.

1-Chloronaphthalene-1-C^{14}. 3.80 g (21.1 mmoles) of 1-naphthylamine-1-C^{14} hydrochloride, 70 ml of water and 1 ml of concentrated hydrochloric acid was heated until the precipitate completely dissolved, 25 ml of concentrated hydrochloric acid added and the solution then quickly cooled. The suspension of 1-naphthylamine-1-C^{14} hydrochloride was cooled to −13°, 4.70 ml of 4.38 N sodium nitrite solution (20.7 mmoles) added (beneath the liquid layer) and the mixture stirred for a further hour while the temperature was kept at from −9 to −12°. The brown solution of the diazo compound was filtered through a porous glass filter (No. 2), cooled in an ice-salt mixture, and added to a freshly prepared hydrochloric acid solution of cuprous chloride (prepared from 5.30 g of copper sulfate by reduction with bisulfite [25] followed by solution in 8 ml of concentrated hydrochloric acid), cooled to 0°. The suspension obtained was placed in a flask with a reflux condenser, heated to 80° (bath temperature) and kept with periodic shaking at 80° for 30 minutes and at 100° for 30 minutes. During this time the evolution of nitrogen completely ceased. The 1-chloronaphthalene-1-C^{14} formed during the reaction was steam distilled off. The distillate was extracted with ether; the ether extract was washed with dilute sodium hydroxide solution and dried with calcium chloride. After evaporation of the ether, the residual oil was distilled from a 10-ml Claisen flask (height of pear column, 5 cm). The 1-chloronaphthalene-1-C^{14} obtained in this way was an almost colorless liquid with b.p. 98-100° (5 mm) and the yield was 1.68 g (49.3%). According to literature data, the boiling point of 1-chloronaphthalene is 104.8° at 5 mm [25]. Into the Claisen flask was placed 2.35 g of inactive 1-chloronaphthalene* and the vacuum distillation repeated. The 1-chloronaphthalene distilled off (2.30 g, b.p. 98-99° at 5 mm) and a further 2.80 g of an inactive preparation was added to the radioactive sample. The 1-chloronaphthalene-1-C^{14} preparation obtained in this way had solid. point −3.8° (according to literature data [6], the solid. point of 1-chloronaphthalene is −2.3°).

Isomerization of 1-chloronaphthalene-1-C^{14} and isolation of 2-chloronaphthalene. The catalysis tube 1 (Fig. 2), made from heat resistant glass (internal diameter 12 mm), had a heating spiral (on top of a layer of asbestos) on the working section with coils arranged so that the variation in temperature along the tube did not exceed 10°. A layer of catalyst (180 mm high) was placed in tube 1 between two layers of broken porcelain; the upper of these (10 mm high) was used to evaporate the 1-chloronaphthalene-1-C^{14}. As the catalyst for the isomerization we used granulated synthetic aluminosilicate catalyst for cracking petroleum.

The 1-chloronaphthalene-1-C^{14} was fed from reservoir 2 into tube 1 by means of compressed air, produced by moving plunger 3. A steady input was thus achieved by maintaining a constant pressure. The end of capillary 4 leading into the catalysis tube 2 was pulled out (however, without reducing the internal diameter of the capillary). This made it possible to reduce the weight of a drop of 1-chloronaphthalene-1-C^{14}, supplied to the evaporation zone, to 6-7 mg. The input rate of hydrogen chloride was controlled with the rheometer 6.

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* The preparation was obtained by recrystallizing distilled technical 1-chloronaphthalene (solid. point −8°) 5 times from anhydrous alcohol at −60° and had b.p. 121° (13 mm) and solid. point −3.3°.

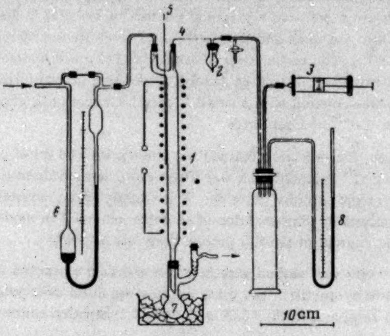

Fig. 2. Apparatus for isomerization of 1-chloronaphthalene-1-C^{14}. 1) Tube with catalyst; 2) reservoir for 1-chloronaphthalene-1-C^{14}; 3) cylinder with plunger; 4) capillary; 5) thermocouple; 6) rheometer; 7) catalyzate receiver; 8) manometric tube.

To remove water contained in the catalyst, tube 1, filled with catalyst, was heated to 250°, while a stream of air was passed through it. Then the stream of air was replaced by a stream of hydrogen chloride, the temperature was raised to 360° over 1 hour and the addition of 1-chloronaphthalene-1-C^{14} begun. The catalyzate was collected in the ice-cooled flask 7.

Experiment 1. The amount of catalyst was 9.45 g. The temperature inside tube 1 was 355-360° (thermocouple 5, placed under the layer of asbestos, was previously calibrated against the readings of a thermometer placed in tube 1). 2.25 g of 1-chloronaphthalene-1-C^{14} was passed through the catalyst over 55 minutes with a hydrogen chloride input rate of 18-20 ml/ min (molar ratio 1-$C_{10}H_7Cl$-1-C^{14} : HCl = = 1 : 3.4). This yielded 2.00 g (89%) of a light yellow catalyzate with solidification point 24.7°. This solidification point corresponded to a 2-chloronaphthalene content of 56% [6].

Experiment 2. 3.68 g of 1-chloronaphthalene-1-C^{14} was passed through 9.00 g of catalyst at 360-365° over 85 minutes. The hydrogen chloride input rate was 20 ml/ min (molar ratio 1-$C_{10}H_7Cl$-1-C^{14} : HCl = 1 : 3.4). The yield of catalyzate was 3.46 g (94%) and the solid. p. 23.7° (55% 2-chloronaphthalene).

The catalyzates obtained in experiments 1 and 2 were cooled to 0° and the crystalline 2-chloronaphthalene filtered off. The filtered liquid mixture of chloronaphthalenes was dissolved in 7.5 ml of anhydrous alcohol and cooled to −40°. The 2-chloronaphthalene thus precipitated was filtered off and washed with 0.7 ml of anhydrous alcohol, cooled to −40°. This operation was performed 5 more times with the cooling temperature gradually lowered to −70°. A total of 2.58 g of 2-chloronaphthalene was isolated. After recrystallization from a mixture of 12 ml of methyl alcohol and 1 ml of water, the 2-chloronaphthalene appeared as lustrous, colorless plates; yield 1.78 g, m.p. 53-54°. According to literature data the melting point of 2-chloronaphthalene is 61° [27].

2-Naphthol. Into a hermetically sealable stainless steel tube of 26.5 ml capacity was placed 0.68 g (4.2 mmoles) of 2-chloronaphthalene and 16.2 ml (12.9 mmoles) of 0.8011 N sodium hydroxide solution. The tube was placed in a rotating autoclave, which was $^1/_3$ filled with water, heated to 365° over 1 hour and kept at that temperature for 40 minutes. The cooled contents of the tube were filtered and acidified with 5 ml of concentrated hydrochloric acid. This yielded 0.48 g (79.5%) of 2-naphthol with m.p. 106-110°.

Similarly, we obtained 0.72 g (73.8%) of 2-naphthol from the remaining 1.10 g of 2-chloronaphthalene.

Model experiments showed that the nitrosation of 2-naphthol of this nature led to considerable tar formation. Therefore the radioactive 2-naphthol obtained was recrystallized from 140 ml of water. The colorless, lustrous plates (0.74 g yield) had m.p. 119.5-120.5°. A melting point of 122-123° is reported in the literature [28].

1-Nitroso-2-naphthol. To a cooled solution of 0.74 g (5.13 mmoles) of 2-naphthol in 9.0 ml of 0.5740 N sodium hydroxide solution (5.16 mmoles) was added a solution of 0.370 g of 95.5% sodium nitrite (5.13 mmoles) in 4.55 ml of water. The mixture was stirred very vigorously and kept at −0.5 to −1.0°, while 3.35 ml of 2 N sulfuric acid solution was added over 2.5 hours and then stirring was continued for a further 1 hour. The 1-nitroso-2-naphthol obtained was filtered off, washed with water until neutral to congo and dried in vacuum. The yield was 0.85 g (96%) and the m.p. 101-104°. According to literature data, 1-nitroso-2-naphthol has m.p. 106° [8].

Cis-o-cyanocinnamic acid. A solution of 0.735 g (18.4 mmoles) of sodium hydroxide in 7.6 ml of water was added to a solution of 0.85 g (4.9 mmoles) of 1-nitroso-2-naphthol and 1.86 g (9.8 mmoles) of p-toluenesulfonyl chloride in 16 ml of toluene heated to 70°. The temperature rose to 90° and the reaction mixture boiled. The boiling was maintained for 15 minutes more and then the dark brown reaction mass was quickly cooled. The alkaline layer was separated and the organic layer extracted three times with 10% sodium hydroxide solution (3 ml portions). On acidifying the filtered alkaline solution, we obtained 0.56 g (66%) of cis-o-cyanocinnamic acid with m.p. 132-134°. Recrystallization from 10 ml of water with charcoal added yielded 0.47 g of acid with m.p. 135-136°. According to literature data, the m.p. of cis-o-cyanocinnamic acid is 137° [9].

Trans-o-carbamidocinnamic acid. A mixture of 0.47 g of cis-o-cyanocinnamic acid, 0.44 ml of concentrated hydrochloric acid and 4.8 ml of water was heated for 35 hours under reflux with a bath temperature of 94-96°. During this time the solution gradually deposited crystals of trans-o-carbamidocinnamic acid, which was filtered off through a steam-heated funnel at the end of the reaction. The yield was 0.33 g (63.5%) and the m.p. 231-232° (with gas evolution). Reprecipitation from a 5% soda solution (with charcoal) yielded 0.31 g of a colorless crystalline product with m.p. 236-237°. According to literature data the m.p. is 239° [10].

Found %: C 62.18, 62.14. $C_{10}H_9O_3N$. Calculated %: C 62.81.

Activity: 1987, 2025 µC/ mole.

Trans-o-aminocinnamic acid. A solution of sodium hypobromite, prepared from 0.234 g (1.52 mmoles) of bromine and 1.50 ml of 2.165 N sodium hydroxide solution (3.24 mmoles) was added over 10 minutes to an ice-cooled solution of 259 mg (1.355 mmoles) of trans-o-carbamidocinnamic acid in 2.38 ml of carbonate-free 2.165 N sodium hydroxide solution (5.16 mmoles) and 3 ml of water in flask 1 (Fig. 3).

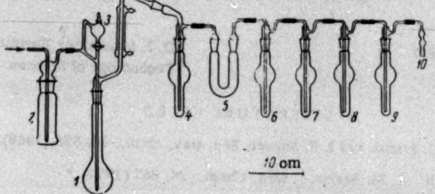

Fig. 3. Apparatus for degradation of trans-o-carbamidocinnamic acid. 1) Reaction flask ; 2) control wash bottle with barium hydroxide solution; 3) dropping funnel; 4) wash bottle with concentrated sulfuric acid; 5) U-tube filled with pieces of pumice impregnated with anhydrous copper sulfate; 6, 7, 8, 9) traps with barium hydroxide solution, 10) tube with ascarite.

The solution was mixed by bubbling through a stream of air, freed from CO_2 by two traps with ascarite. (The absence of CO_2 was checked by the transparency of the barium hydroxide solution in bottle 2). The reaction mixture was kept at 0° for 10 minutes, heated to boiling over 3 hours and boiled for 15 minutes. Air was passed through continuously and the traps 6-9 were filled with 15, 10, 10 and 10 ml respectively of 0.2570 N barium hydroxide solution containing 20 g of barium chloride per liter. To the ice-cooled, dark orange solution in flask 1 was gradually added 3.7 ml of 2.165 N hydrochloric acid from funnel 3. The carbon dioxide thus liberated was flushed through with a stream of air and absorbed in traps 6-9. The U-tube 5, filled with pieces of pumice impregnated with anhydrous copper sulfate, was used to absorb hydrogen chloride flushed out of flask 1 with the air [29].

5.5 liters of air was passed through over a period of 3 hours. The transparency of the solution in trap 9 confirmed the completeness of CO_2 absorption. The amount of carbon dioxide absorbed in the first three traps was determined by titrating the excess barium hydroxide with 0.1 N hydrochloric acid solution. The consumption of the latter was 62.80 ml, which corresponds to 1.357 mmoles (100.2%) of CO_2. The activity of the barium carbonate obtained was 1855 μC/mole. The solution in flask 1 was treated with sodium hydroxide solution until weakly acid to congo and extracted 8 times with ether. The ether extract was dried with baked sodium sulfate and treated with dry hydrogen chloride to give 196 mg (72.5%) of the colorless hydrochloride of trans-o-aminocinnamic acid, which was exactly neutralized with 0.5 N sodium hydroxide solution to yield 120 mg of lemon-yellow trans-o-aminocinnamic acid with m.p. 151.5-152°. According to literature data [10] the m.p. is 158°.

Found %: C 65.70. $C_9H_9O_2N$. Calculated %: C 66.23.

Activity 124.5 μC/mole.

After recrystallization from 4 ml of water the trans-o-aminocinnamic acid had m.p. 153.5-154.5°.

Found %: C 65.62. Activity 125.5 μC/mole.

SUMMARY

1. A method was developed for the degradation of 2-chloronaphthalene, which made it possible to eliminate the carbon atom from position 1 as CO_2. The method is also applicable to other 2-substituted naphthalenes which can be converted into 2-naphthol.

2. We synthesized 1-naphthylamine-1-C^{14} and 1-chloronaphthalene-1-C^{14}, which have not been described previously.

3. In the catalytic isomerization of 1-chloronaphthalene-1-C^{14} at 355-365° the chlorine was mainly transferred to position 2 (by 93.8%). This excludes (under the given conditions) an intermolecular mechanism for the isomerization of monochloronaphthalenes with the intermediate formation of naphthalene.

4. A mechanism was proposed for the intermolecular isomerization of monochloronaphthalenes which assumed the intermediate formation of halonium ions.

Received January 22, 1957

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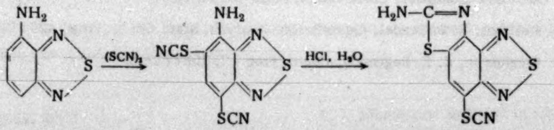
INVESTIGATIONS IN THE FIELD OF 2,1,3-THIODIAZOLE CHEMISTRY

VII. THIOCYANATION OF 4- AND 5-AMINOBENZ-2,1,3-THIODIAZOLES

V. G. Pesin and A. M. Khaletskii

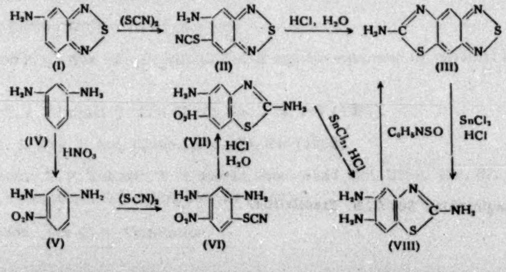
In a previous report [1] we showed that chlorination and bromination of 4-aminobenz-2,1,3-thiodiazole gave 4-amino-5,7-dihalobenz-2,1,3-thiodiazoles; chlorination and bromination of 5-aminobenz-2,1,3-thiodiazole gave, however, 5-amino-6-halobenz-2,1,3-thiodiazoles. Thiocyanation proceeded completely analogously. Thus, thiocyanation of 4-aminobenz-2,1,3-thiodiazole gave a dithiocyano derivative, which was, most probably, 5,7-dithiocyanobenz-2,1,3-thiodiazole, which was converted to a benzthiazole derivative by heating with dilute hydrochloric acid.



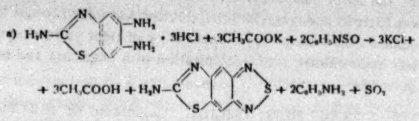
The high reactivity of 4-aminobenz-2,1,3-thiodiazole in halogenation (chlorination, bromination) was particularly well expressed during thiocyanation and the reaction proceeded mainly to form disubstituted derivatives. On reacting equimolecular amounts of the starting materials, part of the 4-aminobenz-2,1,3-thiodiazole did not react; the dithiocyano derivative was formed in approximately 45% yield. When the reactant ratio was calculated so as to give a dithiocyano derivative, the latter was formed in high yield.

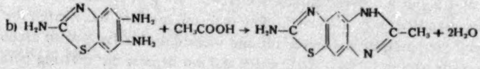
Thiocyanation of 5-aminobenz-2,1,3-thiodiazole (I) gave a 6-thiocyano derivative (II), which was isomerized by heating with dilute hydrochloric acid to 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III), whose structure was proved by synthesis. For this purpose, m-phenylenediamine (IV) was converted to 4-nitro-1,3-diaminobenzene (V), from which 6-thiocyano-4-nitro-1,3-diaminobenzene (VI) was synthesized by thiocyanation. The latter was isomerized to 2,5-diamino-6-nitrobenzthiazole (VII), which was reduced to 2,5,6-triaminobenzthiazole (VIII), a product identical to that obtained by the reductive decomposition of 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III).

Condensation of (VIII) with thionylaniline gave 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III), which was identical to the isomerization product of 5-amino-6-thiocyanobenz-2,1,3-thiodiazole (II).



The synthesis of 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III) by reacting the hydrochloride of 2,5,6-triaminobenzthiazole with thionylaniline in the presence of potassium acetate, i.e. under conditions of benzimidazole ring formation, indicated that the thiodiazole ring closed very rapidly in comparison with the benzimidazole ring, i.e. the rate of reaction (a)





exceeded that of reaction (b).

As is known, o-aminothiocyano derivatives are extremely unstable and, as a rule, are isomerized to the corresponding 2-aminobenzthiazole derivatives at the moment of formation or during isolation or storage. However, the o-aminothiocyano derivatives of benz-2,1,3-thiodiazole were stable and did not change even when boiled with alcohol or benzene; they were isomerized only by heating with dilute hydrochloric acid or with water. Thus, the thiodiazole ring retarded to a certain degree the intermolecular reaction of the amino and thiocyano groups.

Thiocyanation was carried out (by Kaufmann's method [2]) with thiocyanogen, which was formed by the reaction of bromine with ammonium (potassium) thiocyanate in the presence of ammonium (potassium) bromide in an inert solvent medium (methanol) at 0-2°.

EXPERIMENTAL

4-Amino-5,7-dithiocyanobenz-2,1,3-thiodiazole. 5 g of 4-aminobenz-2,1,3-thiodiazole, m.p. 68°, 16 g of ammonium thiocyanate and 100 ml of methyl alcohol was cooled to 0° and a solution of 12 g of bromine in 115 ml of methyl alcohol, saturated with ammonium bromide, was added at this temperature with continuous stirring over a period of 2.5 hours. The reaction mixture was stirred for 4 more hours and left overnight. The precipitate formed was filtered off and washed with methyl alcohol and water to yield 8.45 g of yellow crystals, which melted at 181° after recrystallization; the yield was 96%.

Found %: C 36.60, 36.43; H 1.52, 1.42; N 26.16, 26.05. $C_8H_3N_5S_3$. Calculated %: C 36.23; H 1.13; N 26.41.

7-Thiocyano-4,5-(2'-aminothiazole)-benz-2,1,3-thiodiazole. A mixture of 0.5 g of 4-amino-5,7-dithiocyanobenz-2,1,3-thiodiazole, 100 ml of water and 1.1 ml of 8% hydrochloric acid was boiled for 5 hours, then cooled and neutralized with sodium bicarbonate and the precipitate filtered off and washed with water. We obtained 0.47 g of yellow crystals with m.p. 178-180°, which were boiled with a mixture of 100 ml of water and 8 ml of concentrated hydrochloric acid for 6 hours and the precipitate filtered off and washed with water; this yielded 0.45 g of yellow crystals, which did not melt at 290° and decomposed when heated further. The crystals either did not dissolve or had very low solubility in organic solvents (ether, alcohol, chloroform etc.).

5-Amino-6-thiocyanobenz-2,1,3-thiodiazole (II). 10 g of 5-aminobenz-2,1,3-thiodiazole (I), m.p. 116°, 300 ml of methyl alcohol and 16 g of ammonium thiocyanate was cooled to 0° and a solution of 11.75 g of bromine in 220 ml of methyl alcohol, saturated with ammonium bromide, was added at this temperature with continuous stirring over 4.5 hours. The reaction mixture was then stirred for 3 hours at 0° and left overnight. The precipitate formed was filtered off and washed successively with methyl alcohol and water; we obtained 11.3 g of yellow crystals with m.p. 179-182°, which solidified after melting and melted again at 257-259°. After recrystallization from benzene the crystals had m.p. 188°. The residue from evaporating the methyl alcohol filtrate to dryness was treated with water, filtered and washed with water and 1.3 g of the material was boiled with 10% hydrochloric acid (in the presence of charcoal) for 1 hour, the hot solution filtered and the hot filtrate made alkaline with 25% ammonia solution. The precipitate formed was filtered off and washed with water; we obtained 1.15 g of crystalline benzthiazole derivative (III) (m.p. 260-262°) in 89% total yield.

Found %: N 26.71, 27.46; S 29.96, 29.93. $C_7H_4N_4S_2$. Calculated %: N 27.00; S 30.77.

5,6-(2'-Aminothiazole)-benz-2,1,3-thiodiazole (III). a) 5.6 g of 5-amino-6-thiocyanobenz-2,1,3-thiodiazole (II) was boiled for 2 hours with 125 ml of concentrated hydrochloric acid and 375 ml of water in the presence of charcoal. The hot solution was filtered and excess 25% NH_4 solution was added to the hot filtrate. The precipitate formed was filtered off and washed with water; we obtained 5.3 g of light yellow crystals with m.p. 262°. A second solution in boiling dilute hydrochloric acid, precipitation with ammonia and recrystallization from dilute dioxan (3 : 1) raised the m.p. to 264°.

Found %: N 26.62. 26.86; S 29.92, 30.17. $C_7H_4N_4S_2$. Calculated %: N 27.00; S 30.77.

b) To a mixture of 1.2 g of 2,5,6-triaminobenzthiazole, 1.5 g of potassium acetate and 15 ml of alcohol was added 2.5 ml of thionylaniline, b.p. 198-200°. The reaction mixture was heated for 30 minutes on a boiling water bath and cooled and the precipitate filtered off and washed successively with alcohol and water. We obtained 0.3 g of green crystals with m.p. 260-261°, which did not depress the melting point of an authentic sample. Boiling with dilute hydrochloric acid (in the presence of charcoal) and subsequent precipitation with ammonia solution raised the m.p. to 264°.

2,5,6-Triaminobenzthiazole hydrochloride (VIII). a) A solution of 22.5 g of stannous chloride in 25 ml of concentrated hydrochloric acid was added over a period of 1.5 hours to 5 g of 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III) and 25 ml of hydrochloric acid (d 1.19), which was heated on a boiling water bath and stirred. After 3 hours heating and subsequent cooling, the precipitate was filtered off and washed with concentrated hydrochloric acid. We obtained 6 g of a substance which did not melt on heating to 250-260° but acquired a violet color at this temperature and was soluble in water. For purification, 0.6 g of the hydrochloride was boiled for 15 minutes with 7 ml of concentrated hydrochloric acid and 9 ml of water in the presence of charcoal and then the mixture was filtered hot. To the warm colorless filtrate was added 17 ml of concentrated hydrochloric acid and the fine needles which separated were filtered off and washed with concentrated hydrochloric acid.

Found %: N 19.26, 18.99; Cl 37.11, 36.85. $C_7H_{11}N_4SCl_3$. Calculated %: N 19.34, Cl 36.78.

b) Over a period of 30 minutes 14.8 g of stannous chloride in 25 ml of concentrated hydrochloric acid was added with vigorous stirring to 4 g of 2,5-diamino-6-nitrobenzthiazole in 20 ml of hydrochloric acid (d 1.19) at 100°. The reaction mixture was then heated on a boiling water bath for 3 hours and cooled and the precipitate filtered off, washed with concentrated hydrochloric acid and dried. We obtained 6 g of crystals, which were purified by boiling for $^1/_2$ an hour with a mixture of 40 ml of concentrated hydrochloric acid, 60 ml of water and charcoal; the hot solution was filtered and to the cooled filtrate was added 100 ml of concentrated hydrochloric acid; we obtained 4.7 g of white crystals.

Found %: N 18.92, 18.78; Cl 36.72, 36.78. $C_7H_{11}N_4SCl_3$. Calculated %: N 19.34; Cl 36.78.

4-Nitro-1,3-diaminobenzene (V) was prepared according to literature data [3, 4] by nitration of 1,3-diacetylaminobenzene with subsequent hydrolysis of the 4-nitro-1,3-diacetylaminobenzene.

4-Nitro-6-thiocyano-1,3-diaminobenzene (VI). Over a period of 5 hours, 23.85 g of bromine in 300 ml of methanol saturated with ammonium bromide was added to 20 g of 4-nitro-1,3-diaminobenzene, m.p. 157-159°, 32.6 g of ammonium thiocyanate and 300 ml of methanol stirred vigorously at 0°. After being stirred for 1 hour and left overnight, the precipitate formed was filtered off, washed with methanol and water and dried; we obtained 23.65 g of substance with m.p. 175-176°.

After diluting the filtrate with water and separating the precipitate formed, we obtained a further 5 g of substance with m.p. 143-165°. The substance consisted of crystals which were insoluble in water and readily soluble in many organic solvents and crystallized readily from aqueous alcohol or aqueous acetone; however, the crystals isolated after recrystallization from aqueous alcohol had different properties. Apparently, some kind of conversion had occurred. Heating with dilute hydrochloric acid yielded the corresponding benzthiazole derivative, which we used for purification.

2,5-Diamino-6-nitrobenzthiazole (VII). 5 g of 4-nitro-6-thiocyano-1,3-diaminobenzene, m.p. 175-176°, 700 ml of water and 50 ml of concentrated hydrochloric acid was boiled for 1.5 hours in the presence of charcoal, after which the hot solution was filtered and the filtrate made alkaline with ammonia solution. The orange crystals formed were filtered off and washed with water; we obtained 4.1 g of substance. For analysis, 0.6 g of this substance was again heated with dilute hydrochloric acid (in the presence of charcoal); the hot solution was made alkaline with ammonia solution and the precipitate formed filtered off and washed successively with water and alcohol.

Found %: C 39.91, 40.37; H 3.10, 3.01; N 26.47, 26.43. $C_7H_6O_2N_4S$. Calculated %: C 40.00; H 2.86, N 26.67.

SUMMARY

1. It was found the thiocyanation of 4-aminobenz-2,1,3-thiodiazole gave a high yield (95%) of 4-amino-5,7-thiocyanobenz-2,1,3-thiodiazole, which was converted to (supposedly) 7-thiocyano-4,5-(2'-aminothiazole)-benz-2,1,3-thiodiazole by heating with dilute hydrochloric acid.

2. It was found that thiocyanation of 5-aminobenz-2,1,3-thiodiazole gave a high yield (90%) of 5-amino-6-thiocyanobenz-2,1,3-thiodiazole, which isomerized to 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole when heated with dilute hydrochloric acid.

3. It was found that thiocyanation of 4-nitro-1,3-diaminobenzene gave, in almost quantitative yield, 6-thiocyano-4-nitro-1,3-diaminobenzene, which isomerized to 2,5-diamino-6-nitrobenzthiazole when heated with dilute hydrochloric acid.

4. A practical method for synthesizing 2,5,6-triaminobenzthiazole in high yield was found.

5. It was shown that the hydrochloride of 2,5,6-triaminobenzthiazole reacted with thionylaniline (in the presence of potassium acetate) to form 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole.

6. It was shown that under identical conditions, the thiodiazole ring formed much more readily than the imidazole ring.

7. The reaction of thionylaniline with o-diamines of the aromatic series was extended to include o-diamines of the benzthiazole series, containing an amino group in position 2; in addition, it was shown that o-diamines are capable under certain conditions of reacting with thionylaniline not only as free bases, but also as salts.

Received January 17, 1957

Leningrad Chemical Pharmaceutical Institute

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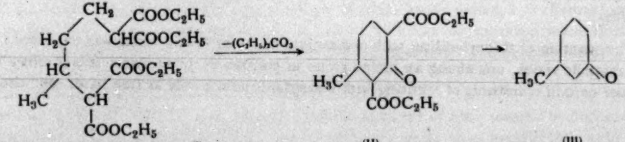
* Original Russian pagination. See C. B. Translation.

INVESTIGATION IN THE FIELD OF THE DIECKMANN REACTION

IV. CYCLIZATION OF THE TETRAETHYL ESTER OF 2-METHYLPENTANETETRACARBOXYLIC-1,1,5,5 ACID

V. I. Zaretskii and N. S. Vul'fson

In continuing the study of the Dieckmann reaction [1], we investigated the cyclization of the tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). It was found that no cyclization of the tetraester (I) occurred in the presence of sodium powder in benzene (the starting tetraester was recovered), but cyclization did occur in the presence of sodium ethylate in an alcohol solution to give a 44.5% yield of 3-methyl-2,6-dicarbethoxycyclohexanone (II). The cyclization was accompanied by the elimination of diethyl carbonate [2,3], which was isolated during the distillation of the reaction product.



(I) (II) (III)

The structure of the ketodiester (II) was confirmed by data from elementary analysis, molecular refraction and its hydrolysis and subsequent decarboxylation to give 3-methylcyclohexanone (III), whose constants agreed with those described in the literature for this substance [4, 6]. The starting tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I) was prepared by condensing 1,3-dibromobutane with sodiomalonic ester. Reaction of stoichiometric amounts of malonic ester and dibromide gave a 12.8% yield of tetraester (I), although 90% of sodium bromide was obtained. By condensing 1 mole of 1,3-dibromobutane with 2 moles of sodiomalonic ester in the presence of a large excess of malonic ester (4 moles) and carrying out the reaction in analogy with the method used by V. P. Gol'mov and B. A. Kazanskii [7], we obtained a 36.9% yield of tetraester (I). A greater excess of malonic ester did not affect the yield of the condensation product.

EXPERIMENTAL

Butanediol-1,3 was prepared by the hydrogenation of technical acetaldol in methanol solution by Hancock's method [8]; the yield, calculated on acetaldehyde, was 36%.

B.p. 80-82° at 2 mm, $n^{20}D$ 1.4415, d^{20}_4 1.0074. According to literature data: b.p. 208-209° at 760 mm, $n^{20}D$ 1.441, d^{20}_4 1.0046 [9].

1,3-Dibromobutane was prepared by the method of Kazanskii and Lukina [10]; the yield was 70%.

B.p. 60-62° at 12 mm, $n^{20}D$ 1.5095, d^{20}_4 1.8062. According to [10]: b.p. 174.5-175.5° at 760 mm, $n^{20}D$ 1.5092, d^{20}_4 1.7904.

Tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). To a solution of sodium ethylate (from 10 g of metallic sodium and 300 ml of anhydrous alcohol) was added 215 g of malonic ester, the solution heated to boiling and stirred and 48 g of dibromobutane-1,3 added to the boiling mass over a period of 2 hours. After the addition of the dibromide, the mass was boiled till it gave a neutral reaction to moist phenolphthalein paper (9-10 hours). The alcohol was distilled off on a boiling water bath (at the end in a vacuum of about 60 mm) and the residue (a suspension) cooled to room temperature, diluted with 200 ml of water and made weakly acid to congo with 25% sulfuric acid. (I) was extracted with ether (2 × 100 ml), the ether extract washed with water until neutral to congo and dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled. We obtained 30.5 g (36.9%) of the tetraester (I) as a slightly yellowish oily liquid.

B.p. 186-192° at 3.5 mm, n^{20}D 1.4450, d$^{20}_{4}$ 1.0883, MR$_D$ 92.74; calc. for keto form 91.94, for enol form 94.034.

Found %: C 57.80; H 7.96. $C_{18}H_{30}O_8$. Calculated %: C 57.75; H 8.02.

Cyclization of tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). To a solution of sodium ethylate (from 16.8 g of sodium and 350 ml of anhydrous alcohol) was added 168.6 g of the tetraester (I) and the solution stirred and boiled for 3 hours. The alcohol was distilled off on a boiling water bath (at the end in a vacuum of 125-170 mm), the residue poured onto 300 g of ice with external cooling with snow and salt keeping the temperature at from −3 to 0°, 200 ml of ether added and the mixture made acid to congo with dilute sulfuric acid (1 : 4) with the temperature kept at from 0 to 3°. The ether layer was separated, the aqueous layer diluted with 400 ml of water, the reaction product extracted with ether (2 × 150 ml) and the combined ether solutions washed with water (4 × 150 ml), 5% soda solution (3 × 50 ml) and again with water. The extract was dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled to give the following fractions: 1st 39° at 200 mm – 45° at 22 mm, 5.5 g; 2nd 116-135° at 2.5 mm, 13.8 g; n^{20}D 1.4620; 3rd 135-140.5° at 2.5 mm, 41.6 g, n^{20}D 1.4710; 4th 140.5-145.5° at 2.5 mm (practically all distilled over at 140.5-142° at 2.5 mm), 17.1 g, n^{20}D 1.4690; residue 23.2 g.

A second distillation of the 1st fraction yielded 1.7 g of diethyl carbonate with b.p. 123-124°, n^{20}D 1.3850; heating with a methanol solution of sodium hydroxide gave a precipitate of Na_2CO_3. According to literature data: b.p. 126°, n^{20}D 1.38456 [11].

The 2nd fraction and the residue were combined and redistilled. This yielded fractions: 1'st 66° at 1.5 mm – 133° at 2 mm, 10.3 g, n^{20}D 1.4527; 2'nd 133-143° at 2 mm, 4.8 g, n^{20}D 1.4688; 3'rd 143° at 2 mm – 189° at 2.5 mm, 13.5 g, n^{20}D 1.4570.

The 3'rd fraction apparently contained mainly unreacted tetraester (I), but fractions 3, 4 and 2' consisted mainly of the cyclic ketoester (II); with an aqueous solution of ferric chloride they gave a violet color. These three fractions were combined and again distilled; the following fractions were collected: 1"st 108-119° at 1 mm, 5.9 g, n^{20}D 1.4695; 2"nd 118.5-124.2° at 1 mm, 39.6 g, n^{20}D 1.4720, d$^{20}_{4}$ 1.0991; 3"rd 124.2-129° at 1 mm, 11.1 g, n^{20}D 1.4705.

Fraction 2": MR$_D$ 64.71, calc. for enol 64.4, for ketone 63.37.

Found %: C 61.30; H 8.05. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.87.

Fraction 3".

Found %: C 61.35; H 8.09. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.87.

Thus, fractions 2" and 3", which were colorless, mobile liquids with an ester smell, were pure 3-methyl-2,6-dicarbethoxycyclohexanone (II).

3-Methylcyclohexanone (III). 62.5 g of potassium hydroxide was dissolved with boiling in 93.5 ml of anhydrous methanol, the hot solution quickly cooled to −4° and 51.1 g of 3-methyl-2,6-dicarbethoxycyclohexanone (II; fraction 2" and 3") added over a period of 20 minutes to the thick mass at a temperature of −4 to 7°, while cooling in ice and salt was continued. The quickly thickening mass was left at 20-22° for 17 days, after which it was dissolved in 200 ml of cold water, acidified with 30% sulfuric acid, a further 50 ml of concentrated sulfuric acid added and the solution steam distilled.

3-Methylcyclohexanone (III) was extracted from the distillate with ether (5 × 100 ml) and the ether solution dried with anhydrous sodium sulfate and distilled; the yield of (III) was 7.8 g (34.9%).

B.p. 164-167.5°, n^{20}D, 1.4455, d$^{20}_{4}$ 0.9127; semicarbazone, m.p. 181-182° (from 70% alcohol). According to literature data: b.p. 165-168°, n^{21}D 1.4450; semicarbazone, m.p. 179° (from CH_3OH) [4], n^{20}D 1.4460; d$^{20}_{4}$ 0.9155 [5]; d$^{20}_{4}$ 0.9136; semicarbazone, m.p. 180° [6].

SUMMARY

We studied the cyclization of the tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid by Dieckmann's method. It was shown that the primary reaction product was 3-methyl-2,6-dicarbethoxycyclohexanone and its structure was confirmed by the production of 3-methylcyclohexanone from it by ketonic cleavage.

Received February 13, 1957

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REACTIONS OF METAL ALCOHOLATE HALIDES

V. THE MECHANISM OF THE REACTION OF MAGNESIUM CARBINOLATE HALIDES WITH ESTERS

I. I. Lapkin, O. M. Lapkina and M. N. Rybakova

Previous investigations [1-3] of magnesium diarylcarbinolate halide reactions with esters of formic acid showed that magnesium diarylcarbinolate halides with unsubstituted ortho-positions form diarylmethyl halides while magnesium diarylcarbinolate halides with all four ortho-positions occupied by methyl groups form hydrocarbons – diarylmethanes. The purpose of this work was to determine the number of ortho-substituents at which hydrocarbons of the diarylmethane type are formed instead of halides.

Investigations carried out with magnesium diarylcarbinolate halides with gradually increasing numbers of ortho-substituents, showed that with less than four substituents this reaction gave diarylmethyl halides. It is possible that diarylmethanes would be formed with three secondary and tertiary radicals, but with more complicated ones than methyl. However, we have not as yet elucidated this problem.

Esters of oxalic acid react with magnesium diarylcarbinolate halides similarly to esters of formic acid. The only difference observed was in relation to magnesium diarylcarbinolate halides with four ortho-positions occupied as the carbinol was regenerated by decomposing the diethyl oxalate reaction products with water and acid.

Examples of malonic ester reactions with magnesium di-o-tolylcarbinolate bromide and with magnesium di-p-tolylcarbinolate bromide confirmed the fact established earlier [1], that, in contrast to esters of formic and oxalic acids, malonic ester formed diarylmethyl ethers with the given carbinolates. The investigation results are given in the table.

The problem of the reaction mechanism of magnesium carbinolate halides with esters arises in connection with the results of the present work and that carried out earlier [1-3]. A solution of this problem would make it possible to forsee new forms of magnesium carbinolate halide reactions and also find an explanation for the nature of many of the anomalies observed in organomagnesium reactions. As is known, G. A. Stadnikov [4] studied the reactions of magnesium alcoholate halides with esters using mainly ethyl acetate. He investigated the reactions of the magnesium alcoholate iodides of benzhydrol, β-methylcyclohexanol and menthol with twice the amount of ethyl acetate and these gave the acetates of the alcohols named. He also established that treatment of ethyl acetate with the magnesium alcoholate iodide of benzhydrol gave dibenzhydryl and benzhydryl ethyl ethers. Stadnikov explained the formation of these ethers and esters in the following way. Organomagnesium compounds react with esters to form first magnesium alcoholate halides of a secondary (if an ester of formic acid is used) or tertiary alcohol. The alcoholate formed reacts with the as yet unreacted starting ester to form the ester of the alcohol synthesized.

$$(R)_2CHOMgI + CH_3COOC_2H_5 \longrightarrow (R)_2CHOCOCH_3 + C_2H_5OMgI$$

According to Stadnikov the ester will then react with magnesium iodide to form an iodide corresponding to the alcohol being synthesized, although Stadnikov did not succeed in isolating an iodide in any of the cases.

$$(R)_2CHOCOCH_3 + MgI_2 \longrightarrow (R)_2CHI + CH_3COOMgI$$

The iodide formed may then lead to three products: 1) reacting with the magnesium alcoholate iodide of the alcohol synthesized, it may give the ether of this alcohol; 2) reacting with the ethylmagnesium iodide found in the reaction mixture, it may give a mixed ester of the alcohol synthesized; and 3) reacting with the unreacted magnesium iodide it may give a hydrocarbon.

According to Stadnikov's data, the above products may be obtained by carrying out the reaction at the boiling point of the ester adding a double quantity of ester, not dropwise, but in one portion and boiling the mixture for many hours (sometimes 40-50 hours).

Reaction components (1 : 1 ratio)	Composition of reaction products (in %)		
	halide	diaryl-carbinol	diarylmethyl ether
MgCl-phenyl-α-naphthylcarbinolate + ethyl formate	86	14	–
MgBr-phenyl-α-naphthylcarbinolate + ethyl formate	88	12	–
MgBr-phenyl-α-naphthylcarbinolate + diethyl oxalate	96	4	–
MgBr-p-xylyl-α-naphthylcarbinolate + ethyl formate	72	28	–
MgBr-di-p-xylylcarbinolate + diethyl oxalate	100	–	–
MgCl-o-tolyl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-o-tolyl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-phenyl-pentamethylphenylcarbinolate + ethyl formate	100	–	–
MgCl-mesityl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-mesityl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgCl-di-p-tolylcarbinolate + diethyl oxalate	70	30	–
MgBr-di-p-tolylcarbinolate + diethyl oxalate	100	–	–
MgBr-di-p-tolylcarbinolate + diethyl malonate	20	–	80
MgBr-di-o-tolylcarbinolate + diethyl malonate	8	–	92
MgBr-dimesitylcarbinolate + diethyl oxalate	–	100	–

The reasons for the formation of such side products as tetraarylethanes and ethers was established correctly in Stadnikov's scheme; however, we cannot agree with the formation schemes he gives for iodides and esters as, for example, esters (benzhydryl acetate and benzhydryl formate) heated with $MgCl_2$ and $MgBr_2$ in an ether solution do not form a halide although, according to our investigations the latter is readily formed by reacting magnesium benzhydrolate chloride with ethyl formate and ethyl oxalate and no halide is formed on heating benzhydryl ethyl ether with $MgCl_2$ and $MgBr_2$.

As mentioned above, we found the conditions for liberating halides by reacting magnesium diarylcarbinolate halides with esters, and the halide yield depended on the character of both the diarylcarbinols and the esters. We consider the mechanism of the reaction between these substances to be as follows.

As is known, the work by Karasch [5] and A. N. Nesmeianov and K. A. Kochetkov [6] made it possible to establish the order of so-called relative electronegativity of various radicals:

$$CH_3 > C_2H_5 > n\text{-}C_3H_7 > n\text{-}C_4H_9 > n\text{-}C_7H_{15} > iso\text{-}C_3H_7 >$$
$$> (CH_3)_2CH-CH_2-CH_2 > \ldots$$

If this idea is carried over to the alkoxyl groups, then we would be able to predict the following order of relative electronegativity of the alkoxyl groups:

$$CH_3O > C_2H_5O > n\text{-}C_3H_7O- > n\text{-}C_4H_9O > n\text{-}C_7H_{15}O >$$
$$> (CH_3)_2CHO > (CH_3)_2CH-CH_2-CH_2O > \ldots$$

If we consider the electronic characteristics of the groups listed, we can then find the mechanism of the given reaction.

The reaction of magnesium alcoholate halides of aliphatic and alicyclic alcohols with ethyl formate gives an initial product of formula (I), which, when treated with dilute acid, is converted into an ester of ortho-formic acid (II).

$$\text{(I) } R-OCH(OC_2H_5)(OMgX) \quad \text{(II) } R-OCH(OC_2H_5)OH$$

As the alkoxyl groups are bonded weakly in acetals and in partial esters of ortho-acids, during the stabilization of this product the most negative alkoxyl group is eliminated in the form of alcohol.

$$R-OCH(OC_2H_5)OH \rightarrow R-O-COH + C_2H_5OH$$

Magnesium alcoholate halides of aliphatic and alicyclic alcohols usually react with esters in this way. The reaction products are esters.

On introducing benzyl or benzylhydryl radicals whose bonds with oxygen are extremely weak, into compound (I), instead of R, compound (I) is stabilized by the following scheme:

$$(C_6H_5)_2CH-O-CH(OC_2H_5)(OMgX) \rightarrow (C_6H_5)_2CHX + CH(OC_2H_5)O_2Mg$$

If alkyl groups, in particular methyl groups, are present in the ortho-position in the phenyl rings, then due to the steric order the halogen cannot migrate to the central carbon atom as the halogens have relatively large atomic volumes. Because of the above, compound (I) is converted by another scheme which results in the formation of a hydrocarbon.

$$[(CH_3)_3C_6H_2]_2CH-O-CH(OC_2H_5)(OMgX) \rightarrow [(CH_3)_3C_6H_2]_2CH_2 + CO(OMgX)(OC_2H_5)$$

The accuracy of this mechanism is confirmed by the fact that when diethyl oxalate is used in the reaction instead of ethylformate, dimesitylmethane could not be formed as hydrogen, capable of migrating to the dimesitylmethyl radical, is absent from the addition product. Therefore, instead of a hydrocarbon being formed, dimesitylcarbinol is again regenerated.

$$[(CH_3)_3C_6H_2]_2CH-O-C(OMgX)(COOC_2H_5)(OC_2H_5) \xrightarrow{H_2O}$$

$$\rightarrow [(CH_3)_3C_6H_2]_2CHOH + CO(OMgX)(COOC_2H_5)$$

The formation of diarylmethyl halides in magnesium diarylcarbinolate halide reactions by the given scheme causes secondary reactions. For example, the formation of symmetrical tetraphenylethane may be explained, doubtlessly, by a Wurtz type of reaction between benzhydryl bromide and metallic magnesium as experimental data indicate [7].

The slow formation of diarylmethyl halides when magnesium diarylcarbinolate halides are heated with diethyl succinate, diethyl malonate or diethyl sulfate results in the formation of ethers. The formation of these compounds may be represented by the usual scheme

$$R_2CHBr + R_2CHOMgBr \rightarrow R_2-CH-O-CHR_2 + MgBr_2$$

It was previously shown [3] that acetone reacted with phenylmagnesium bromide and ethyl benzoate with ethylmagnesium bromide to form magnesium alcoholate bromides of the corresponding tertiary alcohols, which were decomposed by water to tertiary alcohols. If, before decomposing the reaction mixture with water, an equimolecular amount of ethyl formate or ethyl oxalate was added to it, then instead of tertiary alcohols, their dehydration products (unsaturated hydrocarbons) were formed. Such a reaction course is explained by the fact that these esters react with magnesium alcoholate bromides of tertiary aliphatic-aromatic alcohols to form bromides, from which hydrogen bromide is then eliminated and unsaturated hydrocarbons are formed.

Very often deviations from the usual reaction course are observed in reactions of esters with organomagnesium compounds. The mechanism proposed for the reaction of magnesium alcoholate halides with esters makes it possible to explain these anomalies from a single point of view. The appearance of these anomalies is caused by a side reaction between the magnesium alcoholate halides first formed and the esters.

Numerous experiments for studying the reaction of magnesium phenolate halides and magnesium naphtholate halides with esters showed that, in contrast to alcoholates, phenolates and naphtholates do not react with esters.

EXPERIMENTAL*

The reactions between magnesium carbinolate halides and esters were performed under the following conditions. To the diarylcarbinol, dissolved in three volumes of anhydrous ether, was added an ether (3 volumes) solution of the organomagnesium compound, freed from excess magnesium (n-butylmagnesium chloride for the preparation of magnesium carbinolate chlorides and ethylmagnesium bromide for the preparation of magnesium carbinolate bromides). To the ether solution of magnesium carbinolate halide, prepared in this way, was added an equimolecular amount of the ester, dissolved in an equal volume of anhydrous ether. The reaction mixture was heated for 2 hours and decomposed with water and 10% acetic acid. The ether layer was washed with a 10% solution of sodium carbonate and then water until neutral. If ethyl oxalate was used for the reaction, then magnesium oxalate was liberated from the ether layer and precipitated in the aqueous layer. After the ether solution had been dried with baked sodium sulfate, the solvent was distilled off and the product examined after vacuum distillation.

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* Carried out with the participation of the students L. P. Gladkii, L. I. Akoeva, T. N. Povarnitsina and E. I. Terent'eva.

1. Reaction of magnesium phenyl-α-naphthylcarbinolate chloride and bromide with ethyl formate. Starting materials: 6 g ($^1/_{39}$ mole) of phenyl-α-naphthylcarbinol (m.p. 48°), 2.4 g of butyl chloride, 1.9 g of ethyl formate and 1 g of magnesium. Treatment of a sample of the material obtained from the reaction with a saturated solution of silver nitrate in alcohol with heating [8] indicated a chlorine content of 12.06 %(calculated for phenyl-α-naphthylmethyl chloride, 14.03%). Consequently the product obtained contained 86% chloride.

The reaction of magnesium phenyl-α-naphthylcarbinolate bromide with ethyl formate was performed with the same amounts of starting materials (ethyl bromide was used instead of butyl chloride) and lead to the formation of phenyl-α-naphthylmethyl bromide in 88% yield (found %: Br 23.66; calc. 26.59).

Substitution of the ethyl formate by diethyl oxalate increased the yield of phenyl-α-naphthylmethyl bromide to 96%.

Found %: Br 25.80. $C_{17}H_{13}Br$. Calculated %: Br 26.89.

2. Reaction of magnesium p-xylyl-α-naphthylcarbinolate bromide with ethyl formate. p-Xylyl-α-naphthylcarbinol (2,5-dimethylphenyl-α-naphthylcarbinol) was synthesized by reacting p-xylylmagnesium bromide with α-naphthaldehyde. The m.p. was 122° (from a mixture of equal volumes of petroleum ether and toluene). The yield was 52%. The material is not described in the literature.

Found %: C 86.72; H 6.88; OH 6.35. $C_{19}H_{18}O$. Calculated %: C 86.98; H 6.92; OH 6.48.

The addition of an ether solution of ethylmagnesium bromide (the ethylmagnesium bromide content of the ether solution was determined by titration with hydrochloric acid solution) to 7.6 g ($^1/_{40}$ mole) of carbinol gave the magnesium carbinolate bromide, to which ethyl formate (1.9 g) was then added. After the usual operations of heating, decomposing the reaction mixture and distilling off the solvent, a sample of the material obtained was heated with a saturated alcohol solution of silver nitrate. The p-xylyl-α-naphthylmethyl bromide content was 72%.

Found %: Br 17.60. $C_{19}H_{17}Br$. Calculated %: Br 24.57.

3. Reaction of magnesium di-p-xylylcarbinolate bromide with diethyl oxalate. Di-p-xylylcarbinol (2,5,2',5'-tetramethylbenzhydrol) was prepared by reacting p-xylylmagnesium bromide with ethyl formate. The m.p. was 144° (from toluene). The yield was 48%. The material is not described in the literature.

Found %: C 84.70; H 8.42; OH 6.5. $C_{17}H_{20}O$. Calculated %: C 84.95; H 8.39; OH 7.1.

Part of the carbinol obtained was converted into the magnesium carbinolate bromide by the addition of a definite amount of an ether solution of ethylmagnesium bromide. Diethyl oxalate was then added to the carbinolate. The other reaction conditions are described above. When the solvent had been distilled off, the di-p-xylylmethyl bromide (not described in the literature) crystallized and was recrystallized from petroleum ether. The m.p. was 95-96°.

Found %: Br 26.17. $C_{17}H_{19}Br$. Calculated %: Br 26.35.

4. Reaction of magnesium o-tolyl-α-naphthylcarbinolate chloride and bromide with ethyl formate. o-Tolyl-α-naphthylcarbinol, which is not described in the chemical literature, was synthesized by the reaction of o-tolylmagnesium bromide with α-naphthaldehyde. The m.p. was 120-121° (from a mixture of petroleum ether and benzene). The yield was 48%.

Found %: C 86.87; H 6.41; OH 6.2. $C_{18}H_{16}O$. Calculated %: C 87.07; H 6.50; OH 6.8.

The carbinol (6.2 g), dissolved in three volumes of anhydrous ether, as described above, was converted into magnesium carbinolate chloride by the addition of an ether solution of butylmagnesium chloride, and then treated with an ether solution of ethyl formate (1.9 g). The o-tolyl-α-naphthylmethyl chloride (not described in the literature) obtained crystallized and was purified by recrystallization from petroleum ether. The m.p. was 91°.

Found %: Cl 13.01. $C_{18}H_{15}Cl$. Calculated %: Cl 13.29.

Under similar conditions and with the same amounts ($^1/_{40}$ of a mole) of starting materials (ethyl bromide was used instead of butyl chloride) magnesium o-tolyl-α-naphthylcarbinolate bromide was reacted with ethyl formate. The only reaction product was o-tolyl-α-naphthylmethyl bromide with m.p. 94° (from petroleum ether, which was obtained for the first time).

Found %: Br 25.21. $C_{18}H_{15}Br$. Calculated %: Br 25.68.

5. Reaction of magnesium mesityl-α-naphthylcarbinolate chloride and bromide with ethyl formate. Mesityl-α-naphthylcarbinol, which has not been described previously, was synthesized by the reaction of mesitylmagnesium bromide with α-naphthaldehyde. The m.p. was 131° (from a mixture of petroleum ether and toluene). The yield was 33%.

Found %: C 86.72; H 7.18; OH 5.8. $C_{20}H_{20}O$. Calculated %: C 86.93; H 7.30; OH 6.1.

The conditions of the reaction of magnesium mesityl-α-naphthylcarbinolate chloride with ethyl formate and also magnesium mesityl-α-naphthylcarbinolate bromide with the same ester are described above. $^1/_{40}$ mole amounts of the materials required for the reaction (carbinol, butyl chloride or ethyl bromide, magnesium and ethyl formate) were used. The only product of the first reaction was mesityl-α-naphthylmethyl chloride, which was obtained for the first time. The m.p. was 98° (from petroleum ether).

Found %: Cl 11.70. $C_{20}H_{19}Cl$. Calculated %: Cl 12.03.

The product of the second reaction was mesityl-α-naphthylmethyl bromide, which also has not been described previously. The m.p. was 100° (from petroleum ether).

Found %: Br 23.25. $C_{20}H_{19}Br$. Calculated %: Br 23.56.

6. Reaction of magnesium 2,3,4,5,6-pentamethylbenzhydrolate bromide with ethyl formate. 2,3,4,5,6-Pentamethylbenzhydrol was prepared by the reaction of pentamethylphenylmagnesium bromide with benzaldehyde. The m.p. was 105°. A m.p. of 107° is reported in the literature [9]. The reaction conditions for magnesium 2,3,4,5,6-pentamethylbenzhydrolate bromide with ethyl formate are described above. Evaporation of the solvent yielded for the first time 2,3,4,5,6-pentamethylbenzhydryl bromide, which crystallized and had a constant m.p. of 98° after recrystallization from petroleum ether.

Found %: Br 24.80. $C_{18}H_{21}Br$. Calculated %: Br 25.19.

7. Reaction of magnesium di-p-tolylcarbinolate chloride and bromide with diethyl oxalate. Di-p-tolylcarbinol was prepared under the normal Grignard conditions by the reaction of p-tolylmagnesium bromide with ethyl formate. The m.p. was 72°. For this carbinol a m.p. of 71° is reported in the literature [10]. The reaction of magnesium di-p-tolylcarbinolate chloride with diethyloxalate was performed as in the previous experiments with $^1/_{40}$ mole amounts of the starting materials. The di-p-tolylmethyl chloride content of reaction product was 70% (found %: Cl 10.80; calc. 15.73). To convert the unreacted carbinol into chloride and to isolate the chloride in a pure form, the reaction product was dissolved in petroleum ether and a stream of dry hydrogen chloride passed through the solution. The di-p-tolylmethyl chloride isolated had m.p. 42° (from petroleum ether).

Found %: Cl 15.52. $C_{15}H_{15}Cl$. Calculated %: Cl 15.73.

In contrast to the magnesium carbinolate chloride, the magnesium di-p-tolylcarbinolate bromide was completely converted into di-p-tolylmethyl bromide by reaction with diethyl oxalate. The m.p. of the product was 49° (from petroleum ether) [11].

Found %: Br 28.73. $C_{15}H_{15}Br$. Calculated %: Br 29.04.

8. Reaction of magnesium di-p-tolylcarbinolate bromide and magnesium di-o-tolylcarbinolate bromide with diethyl malonate. As a result of the first reaction, evaporation of the solvent and the malonic ester residue yielded a product which contained 20% of di-p-tolylmethyl bromide (found %: Br 5.8; calc. 29.04). No carbinol content was found. This product was vacuum distilled. The bulk of the material distilled over in the range 228-238° at 8 mm. Recrystallization from a mixture of petroleum ether and toluene (1 : 1) gave for the first time di-p-tolylmethyl ether with m.p. 186°.

Found %: C 88.41; H 7.35. $C_{30}H_{30}O$. Calculated %: C 88.63; H 7.44.

The second reaction (magnesium di-o-tolylcarbinolate bromide with diethyl malonate) was carried out similarly to the first and gave the following results: the di-o-tolylmethyl bromide content of the reaction product was 8% (found %: Br 2.3; calc. 29.04); carbinol was not found but there was a 92% content of di-o-tolylmethyl ether, which has not been described previously in the literature. The m.p. of the latter material was 172° (from a mixture of petroleum ether and toluene).

Found %: C 88.39; H 7.30. $C_{30}H_{30}O$. Calculated %: C 88.63; H 7.44.

SUMMARY

1. The study of the reaction of magnesium diarylcarbinolate halides with esters was continued. It was established that only those magnesium diarylcarbinolate halides which have all four ortho-positions occupied by alkyl groups form diarylmethanes with esters of formic acid, while with a lower degree of substitution these reactions give diarylmethyl halides.

2. New examples were used to show that on reaction with malonic esters, magnesium diarylcarbinolate halides are converted to diarylmethyl ethers.

3. It was established that magnesium phenolate bromides and magnesium naphtholate bromides do not react with the esters of formic, oxalic, sulfuric and succinic acids, taken in equimolecular amounts and under the usual reaction conditions.

4. We studied the reaction mechanism of magnesium alcoholate halides with esters.

Received January 8, 1957

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MODELS OF THE MICROSTRUCTURES OF PROTEIN

III. THE STRUCTURE OF PHENYLALANINE ANHYDRIDE DERIVATIVES

L. N. Akimova, I. P. Kuranova and N. I. Gavrilov

In a previous report [1] it was shown that N-aminoacyl derivatives of phenylalanine anhydride were formed especially smoothly and in good yield on treating phenylalanine anhydride with acid chlorides of amino acids. Previously, study of the behavior of N-aminoacyl derivatives of glycine anhydride had shown their exceptional stability in an alkaline medium and particular behavior to hydrazine treatment [2]. This consisted of: 1) the addition of hydrazine at the CO-groups of the phthalyl blocking group when the reaction was carried out in ether or alcohol in the cold, 2) the elimination of the phthalyl group when heated in alcohol and 3) the opening of the diketopiperazine ring to form a phthalyltripeptide hydrazide, without breaking the acyl bond.

In this work we studied the properties of phenylalanine anhydride derivatives and showed how readily they were hydrolyzed by treatment with aqueous and alcohol solutions of alkali and hydrazine. In this way, using the aminoacyl derivatives of two anhydrides (glycine anhydride and phenylalanine anhydride) as examples, we first noticed the effect of the amino acid composition of the anhydride and acyl group on the properties of these derivatives.

The effect of the amino acid composition on the stability of N-aminoacyl and cyclic bonds was noted when investigating the properties of the amino acid anhydride derivatives that we synthesized. It was known, for example, that when treated with 4% NaOH in the cold, glycine anhydride is quantitatively converted to glycylglycine in 20 minutes (Fischer). The aminoacyl derivatives of this anhydride (in which the aminoacyls were phthalylglycyl-, phthalylalanyl-, phthalylvalyl- and phthalylleucyl-) were decomposed to acyltripeptides only after standing for 24 hours under these conditions. In contrast to glycine anhydride, the phenylalanine anhydride that we studied was found to be exceptionally stable. It decomposed (to amino acid) at the −NH−CO bond after heating for 4 hours with 4% NaOH. However, the introduction of amino acid radicals into the molecule of this anhydride made the −NH−CO bond in the ring less stable. Thus, in contrast to phenylalanine anhydride which was decomposed only after prolonged heating, its aminoacyl derivatives were decomposed with 4% NaOH even in the cold. This instability of aminoacyl derivatives of phenylalanine anhydride (in which the aminoacyls were phthalylglycyl-, -alanyl-, -valyl- and -leucyl-) was confirmed by the isolation of phthalyltripeptides from copper biuret complexes and by the capacity of these anhydride derivatives to break down under alkali treatment when titrated in alcohol (by Willstätter's method).

From the given data it follows that the stability of the cyclic bond in aminoacyl anhydrides depends not only on the amino acid composition of the anhydride, but also on the amino acids in the side aminoacyl group. Thus, the stability* of the cyclic bond decreases in the order: N,N'-diphthalylglycyl-, N,N'-diphthalylalanyl-, N,N'-diphthalylvalyl- and N,N'-diphthalylleucyl-phenylalanine anhydrides.

In contrast to the readily decomposed aminoacyl derivatives of phenylalanine anhydride, the same (according to the amino acid composition of the aminoacyls) derivatives of glycine anhydride are exceptionally stable. Thus, the stability of the −NH−CO bond in an isolated ring and in a ring with an N-aminoacyl form of bond was different and depended on the amino acid in the ring and the aminoacyl groups. The stability of the N-acyl and N-aminoacyl bond was, however, directly dependent on the amino acid composition of the anhydride. This was particularly well illustrated by studying the reaction products of anhydride derivatives with hydrazine. Thus, the N-aminoacyl derivatives of glycine anhydride had a more stable bond between the amino acid and diketopiperazine nitrogen than had the derivatives of phenylalanine anhydride. This made it possible for us to use hydrazine to remove the phthalyl blocking group of the N-aminoacyl derivative of glycine anhydride – N,N'-diphthalylglycyl-glycine anhydride. The N-aminoacyl derivatives of phenylalanine anhydride offer a completely different picture. Here the hydrazine effect was limited and consisted of only a specific effect on the N-aminoacyl bond, with the amino acid composition of the acyl group not affecting the specificity of the hydrazine action. Thus, when treated with hydrazine, N,N'-diphthalylglycyl-phenylalanine anhydride, like N,N'-diphthalylalanyl-, phthalylvalyl- and phthalylleucyl-phenylalanine anhydrides, split off aminoacyl groups and not the phthalyl blocking group. In this way, the factor determining the stability of acyl and N-aminoacyl bonds was the amino acid composition of the anhydride.

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* According to the rate of formation of copper biuret complexes.

We had shown previously [3] that, when N-benzyldipeptides were heated in nitrobenzene or glycol, depending on their amino acid composition, they were converted quantitatively to N-benzyldiketopiperazines. We showed the effect of the amino acid composition on the system of conjugated functional groups of amino acids and peptides, using also N-benzyltripeptides [4]. Actually, this effect of amino acids on the properties of N-benzylpeptides was combined with the effect of the benzyl blocking group, which consisted of an increase in the carbonyl functions of the carboxyl. Here, however, the effect of the amino acid composition dominated the effect of the benzyl group. Thus, heating N,N'-dibenzylglycyl-glycyl-glycine gave a diketopiperazine and eliminated N,N'-dibenzylglycine while heating N,N'-dibenzylleucylglycyl-glycine gave N-dibenzylleucine and glycine anhydride. N-benzyltripeptides, which include phenylalanine as the terminal amino acid, formed aminoacyl anhydrides most readily.

Thus, the N-aminoacyl type of bond as one of the chemical bonds of diketopiperazine with amino acids and their derivatives, cannot be studied or examined separately, isolated from the amino acids which participate in its formation.

EXPERIMENTAL

1. N,N'-Diphthalylglycyl-phenylalanine anhydride. 2.27 g (0.0077 mole) of phenylalanine anhydride and 3.44 g (0.016 mole) of phthalylglycine acid chloride were heated in 70 ml of anhydrous xylene. Over 1 hour the bulk of the solid dissolved. Heating was continued for a further 2 hours. The reaction mixture was cooled, the precipitate of unreacted phenylalanine anhydride (0.35 g) filtered off and the xylene filtrate concentrated in vacuum. The crystals, which formed when petroleum ether was added, were filtered off and dried in a vacuum desiccator. The weight was 3.6 g (80%). The m.p. was 243-250°. The substance is not described in the literature. It was readily soluble in chloroform, benzene, xylene and nitrobenzene, but insoluble in water. Under the microscope the crystals from benzene and nitrobenzene appeared as little envelopes. The biuret reaction was positive after the material had stood with alkali. The ninhydrin and picric acid reactions were negative.

Found %: C 68.47; H 4.24; N 8.33. $C_{38}H_{28}O_8N_4$. Calculated %: C 68.25; H 4.18; N 8.36.

To prove the structure we examined the amino acid composition by paper chromatography, the reaction with hydrazine and the biuret reaction.

a) Investigation of amino acid composition. The material was hydrolyzed for 48 hours with 20% hydrochloric acid. Glycine and phenylalanine were found on the paper chromatogram of the hydrolyzate (solvent: butanol–water–acetic acid).

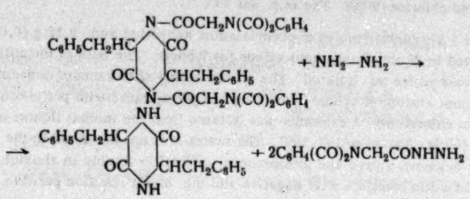
b) Reaction with hydrazine hydrate. 0.1 ml of hydrazine hydrate was added to 0.1 g of N,N'-diphthalylglycyl-phenylalanine anhydride, dissolved in 10 ml of chloroform. After 1 hour, the precipitate was filtered off, washed with absolute ether and dried in a vacuum desiccator. The weight was 0.014 g. The m.p. was 301°.

The precipitate was phenylalanine anhydride. The phthalylglycyl hydrazide, which was isolated by concentrating the chloroform filtrate, was hydrolyzed for 26 hours with 10% HCl. Only glycine was found on the chromatogram (solvent: butanol– water–acetic acid).

Found %: N 23.98. $C_{10}H_9O_3N_3$. Calculated %: N 24.13.

The reaction proceeded quantitatively by scheme 1.

Scheme 1



c) Investigation of copper biuret complex. To 0.5 g of N,N'-diphthalylglycyl-phenylalanine anhydride was added 10 ml of 4% NaOH solution and 4% $CuCl_2$ solution until a permanent precipitate of $Cu(OH)_2$ appeared. The mixture was agitated on a rocker for one day and then filtered through a paper filter to remove the $Cu(OH)_2$ from the solution. The absorption spectrum of the copper complex was plotted. The absorption maximum was at 545 mμ (table). Then the copper complex was decomposed with 10% hydrochloric acid. The precipitate formed was filtered off, washed with water and dried. The weight was 0.19 g. The m.p. 138°.

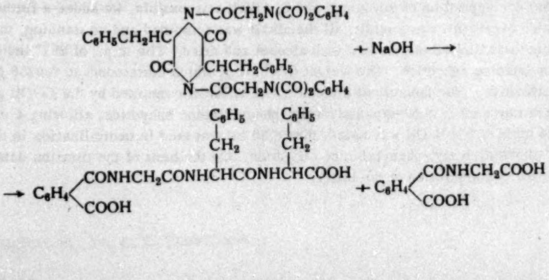
Found %: N 8.37. $C_{28}H_{27}O_7N_3$. Calculated %: N 8.11.

Spectrophotometric Data on the Solutions of the Copper Biuret Complexes

Wave-length λ (in mμ)	Values of optical densities ε		Wavelength λ (in mμ)	Values of optical densities ε	
	N,N'-diphthalylglycyl-phenylalanine anhydride	N,N'-diphthalylalanyl-phenylalanine anhydride		N,N'-diphthalylglycyl-phenylalanine anhydride	N,N'-diphthalylalanyl-phenylalanine anhydride
470	0.258	0.237	560	0.676	0.532
480	0.342	0.300	565	0.652	0.523
490	0.392	0.350	570	0·616	0.490
500	0.428	0.428	575	0.576	0.490
510	0.458	0.462	580	0.558	0.478
520	0,560	0.500	590	0.534	0.440
530	0.658	0.545	600	0.498	0.390
540	0.682	0.543	610	0.432	0.333
545	0.702	0.548	620	0.360	0.290
550	0.700	0.543	630	0.342	0.243
555	0.682	0.530	640	0.282	0.210

Paper chromatographic analysis of the hydrolyzate revealed only two amino acids – glycine and phenylalanine. Thus, the liberation of phthaloylglycyl-phenylalanyl-phenylalanine indicates alkaline decomposition during the biuret reaction proceeding by scheme 2.

Scheme 2



2. N,N'-Diphthalylalanyl-phenylalanine anhydride. a) Phthalylalanyl acid chloride was prepared by the directions for phthalylglycyl acid chloride. From 5 g of phthalylalanine and 5 g of phosphorous pentachloride we obtained 5 g of the acid chloride (90%). The m.p. was 77°.

b) A mixture of 1.3 g (0.0044 mole) of phenylalanine anhydride and 2.12 g (0.0088 mole) of phthalylalanyl acid chloride was heated in 80 ml of anhydrous xylene for 2 hours. The bulk of the solid dissolved. 0.2 g of unreacted phenylalanine anhydride was isolated. The oil remaining after vacuum concentration of the solution was dissolved in the minimum amount of xylene by heating and precipitated with petroleum ether. The precipitate was recrystallized from chloroform. A substance was isolated from the mother liquors on adding petroleum ether. The weight was 1.6 g (62%). The m.p. 197-205°. The material is not described in the literature. It was readily soluble in chloroform, benzene, xylene and nitrobenzene, difficultly soluble in alcohol and insoluble in water. The picric acid and ninhydrin reactions were negative and the biuret reaction positive.

Found %: C 68.94; H 4.91; N 7.94. $C_{40}H_{32}O_8N_4$. Calculated %: C 68.98; H 4.59; N 8.05.

a) Investigation of the amino acid composition revealed alanine and phenylalanine.

b) Reaction with hydrazine. 0.1 ml of hydrazine hydrate was added to a solution of 0.1 g of N,N'-diphthalylalanyl-phenylalanine anhydride in 10 ml of chloroform. The precipitate was filtered off and washed with alcohol. The m.p. of 301° and the properties of the substance isolated indicated that it was phenylalanine anhydride. The phthalylalanyl hydrazide, obtained by concentrating the chloroform filtrate, was hydrolyzed for 26 hours with 10% hydrochloric acid. A paper chromatogram of the hydrolyzate showed only alanine.

Found %: N 17.91. $C_{11}H_{11}O_3N_3$. Calculated %: N 18.02.

Thus, the reaction of N,N'-diphthalylalanyl-phenylalanine anhydride with hydrazine proceeded by scheme 1.

c) The copper biuret complex of N,N'-diphthalylalanyl-phenylalanine anhydride was prepared as described for N,N'-diphthalylglycyl-phenylalanine anhydride. The absorption maximum lay at a wavelength of 545 mμ. Decomposition of the copper biuret complex by acidification with 10% hydrochloric acid yielded 0.15 g of a substance with m.p. 125°. A paper chromatogram of the hydrolyzate (hydrolysis with 10% hydrochloric acid for 24 hours) revealed phenylalanine and alanine.

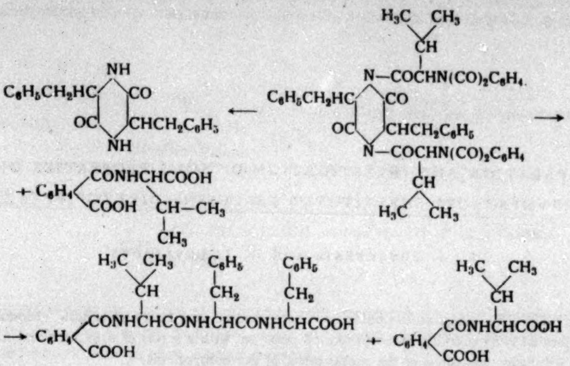
Found %: N 8.15. $C_{29}H_{29}O_7N_3$. Calculated %: N 7.90.

The isolation of phthaloylalanyl-phenylalanyl-phenylalanine on decomposing the copper complex, confirms the decomposition of N,N'-diphthalylalanyl-phenylalanine anhydride under the effect of alkali (under the conditions of the biuret reaction) by scheme 2.

Titration (by the Willstätter method) of phthalylalanylglycine. A 0.1232 g sample was dissolved in 10 ml of 96% ethyl alcohol. It was titrated with 0.1 N alcoholic alkali in the presence of thymolphthalein. The amount of alkali consumed in the titration was 8.96 ml. The theoretical amount of 0.1 N alkali, calculated for phthalylalanylglycine, allowing 2 moles per mole of glycine, was 8.92 ml. Thus, during the titration with alkali the phthalyl group was opened to a phthaloyl one.

Decomposition of N,N'-diphthalylvalyl-phenylalanine anhydride under the effect of 0.1 N alcoholic alkali under titration conditions (by Willstätter's method). A 0.1759 g sample was dissolved in 5 ml of 96% ethyl alcohol. The theoretical amount of alkali for the decomposition of this compound by two moles of alkali (M 752.79) equalled 4.67 ml; the titration required 4.62 ml.

Since further decomposition of this compound by alkali was possible, we added a further 4.62 ml of alkali and left the solution overnight. As a result, all the alkali was consumed and on standing, the solution deposited a precipitate, which was filtered off, washed with alcohol and dried. The m.p. of 291° indicated that the precipitate was phenylalanine anhydride. The weight was 0.01 g, which corresponds to 0.0256 g of N,N'-diphthalylvalyl-phenylalanine anhydride. The theoretical amount of 0.1 N NaOH consumed by the COOH groups liberated in the hydrolysis of this amount of N,N'-diphthalylvalyl-phenylalanine anhydride, allowing 4 moles, was 0.85 ml. As a total of 9.24 ml of 0.1 N NaOH was added, then 8.39 ml was used in neutralization in the decomposition of 0.1503 g of N,N'-diphthalylvalyl-phenylalanine anhydride. On the basis of the titration data, the following scheme is put forward for the decomposition of the latter.



SUMMARY

1. We described the synthesis of N-aminoacyl derivatives of phenylalanine anhydride: N,N'-diphthalylglycyl- and N,N'-diphthalylalanyl-phenylalanine anhydrides.

2. The hypothesis put forward previously on the mechanism of the removal of the N-aminoacyl groups from these compounds by hydrazine treatment was confirmed.

3. Their behavior was studied under the conditions of a biuret protein reaction (4% NaOH) and to show their decomposition under alkali treatment to phthaloylglycyl-phenylalanyl-phenylalanine and phthaloylalanyl-phenylalanyl-phenylalanine.

4. On the basis of titration data (by Willstätter's method) a decomposition scheme for N,N'-diphthalylvalyl-phenylalanine anhydride under alkali treatment is proposed.

Received January 7, 1957

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* Original Russian pagination. See C. B. Translation.

PREPARATION AND INVESTIGATION OF SOME PROPERTIES OF N-MONOAMINOACYL SUBSTITUTED SARCOSINE DIKETOPIPERAZINES

N. A. Poddubnaia and G. I. Lavrenova

Monoaminoacyl derivatives of amino acids have been studied very little up to now. Monoacyldiketopiperazine was first prepared [1] by reacting diacetyldiketopiperazine with a series of aliphatic and mixed amines in ether and benzene solutions, regardless of the molar ratios of the components.

In this work we synthesized a series of mixed N-monoaminoacyl derivatives of diketopiperazines, containing one tertiary nitrogen atom, in order to study systematically the rules connected with the appearance of such atoms in a molecule. In addition, the introduction of sarcosine into a molecule of the compound being investigated is interesting in itself as this amino acid, together with N-methylvaline and proline, form part of the antibiotic – actinomycin C [2]. The structure of this antibiotic has not yet been proved conclusively but, according to the authors' data, treatment of the compound with hydrazine hydrate gives N-methylvalyl-sarcosine anhydride and leucylproline anhydride, which may be due to rupture of the aminoacyl bond, as was also confirmed in our work.

The sarcosine anhydrides were acylated with the acid chlorides of N-phthalyl substituted amino acids, which were very stable to heating and the diketopiperazines were acylated by them quite well. The N-phthalylaminoacyl derivatives and their properties are given in Table 1.

TABLE 1

Name of compound	Melting point	Yield (in %)
N-Phthalylglycyl-sarcosyl-D,L-valine anhydride	184-185*	63
N-Phthalyl-D,L-valine-sarcosyl-glycine anhydride	187-188*	50
N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride. .	177	20
N,N'-Diphthalylglycyl-glycyl-D,L-valine.	195	58

The properties of the compounds obtained were quite similar to those of N,N'-diphthalyl derivatives of glycine diketopiperazines [3-5]. N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride, whose amino acid composition is similar to that of N-phthalylglycyl-sarcosine-D,L-valine anhydride, had properties characteristic of aminoacyls.

The slow formation of copper complexes* was characteristic of all mono- and diaminoacyl derivatives of diketopiperazines and a displacement of the maximum was observed for both in relation to free tripeptides (Table 2).

As the data in Table 2 show, all monoaminoacyl derivatives of sarcosine anhydrides gave biuret complexes with an absorption maximum close to that of dipeptides, which was apparently due to the presence of a tertiary nitrogen atom as N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride formed a copper complex with an absorption maximum characteristic of tripeptides.

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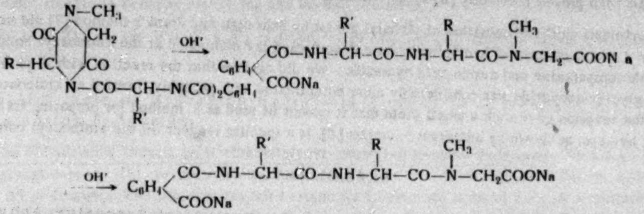
* Due to decomposition of the diketopiperazine ring.

The decomposition of N-phthalylaminoacyl derivatives in an alkaline medium may be shown in the following way.



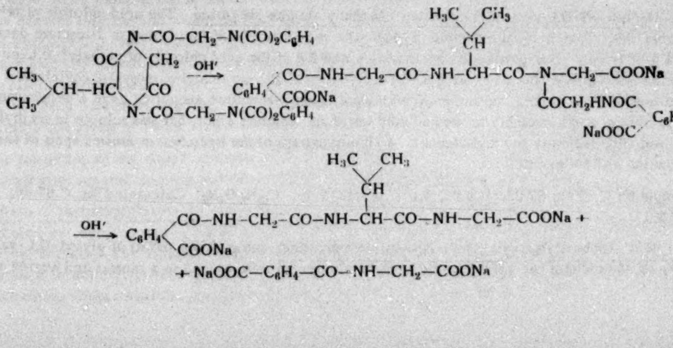
A similar decomposition scheme was proved by synthesizing the aminoacyl derivative of N-phthaloyl-glycyl-D,L-valyl-sarcosine obtained in the decomposition and by identifying it with the compound of similar structure isolated from a solution of the copper complex.

TABLE 2

Name of tripeptide	Absorption maximum λ(m μ)	Name of aminoacyl	Absorption maximum λ(m μ)
Glycyl-D,L-valyl-sarcosine	660 (with excess copper)	N-Phthalylglycyl-sarcosyl-D,L-valine anhydride	640
D,L-Norleucyl-D,L-phenylalanyl-sarcosine	660 (with excess copper)	N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride	640
D,L-Valyl-glycyl-sarcosine	660 (with excess copper)	N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride	640
Glycylglycyl-D,L-valine	582	N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride	560

The phthaloyl group, formed as a result of partial hydrolysis of the phthalyl group, promoted the formation of a biuret complex. After prolonged standing with alkali, the absorption maximum was slowly displaced into the long wavelength region of the spectrum and possibly at the same time the phthaloyl radical was eliminated to form tripeptides, containing sarcosine as the terminal amino acid.

N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride was decomposed with 2 N NaOH by the following scheme, which was also proved by synthesis.



The acyl group at the tertiary nitrogen atom was unstable and was eliminated in an alkaline medium [4]. The substance synthesized, N-phthaloylglycyl-glycyl-D,L-valine, according to its absorption spectrum and chromatogram, corresponded to the tripeptide isolated after the decomposition of the copper complex. Such a decomposition had been proved previously [6] by determining the amount of free carboxyl groups.

Experiments on the elimination of phthalyl groups by Scheehan and Frank's method [7] did not give positive results as a 1 molar solution of hydrazine hydrate decomposed the compound at the aminoacyl bond to give the original diketopiperazine and amino acid hydrazide. We did observe that the reaction with N-phthalyl-D,L-valyl-sarcosyl-glycine anhydride was considerably more complicated and, probably, formed an aminoacyl derivative; however, the reaction gave such a small yield that it cannot be used as a method for preparing free aminoacyls. Hydrazine hydrate, as shown by numerous examples [8], is a specific reagent for the aminoacyl bond.

EXPERIMENTAL

I. Synthesis of N-Monophthalylaminoacyl Derivatives of Sarcosine Anhydrides

1. N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride. a) Acid chloride of N-phthalyl-D,L-valine [9]. 2 g (0.008 mole) of phthalyl-D,L-valine was ground in a mortar with 1.7 g (0.008 mole) of phosphorous pentachloride and the mixture heated with 30 ml of absolute benzene on an oil bath at 60°. After the solid had dissolved the solution was heated for a further 1 hour. The benzene was distilled off in vacuum and the oil formed (1.3 g) used for the preparation of the anhydride.

b) N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride. A mixture of 0.6 g (0.003 mole) of sarcosyl-glycine anhydride and 1.3 g (0.005 mole) of the acid chloride of phthalyl-D,L-valine was heated in 30 ml of absolute xylene at the boiling point of the solvent for 4 hours. After evaporation of the solvent, the crystals were washed with ether to remove phthalyl-D,L-valine and its acid chloride and with water to remove diketopiperazine. The yield was 1.08 g (65%). After a recrystallization from benzene, the melting point was 187-188°. A chromatogram of the hydrolyzate in butanol—water—acetic acid medium (4 : 5 : 1) showed three spots — sarcosine, valine and glycine.

Found %: C 59.88, 59.84; H 5.39, 5.44 ; N 11.78, 11.73. $C_{18}H_{19}O_5N_3$. Calculated %: C 60.5; H 5.32; N 11.76.

2. N-Phthalyl-glycine-sarcosine-D,L-valine anhydride. The acid chloride of N-phthalylglycine was prepared by the method of Scheehan and Frank [7]. The m.p. was 81-83° (according to literature data: m.p. 83-85°). 2 g (0.009 mole) of the acid chloride of N-phthalylglycine and 1.5 g (0.009 mole of sarcosyl-D,L-valine anhydride was heated under the conditions given above for 5 hours. After evaporation of the solvent, the oil rapidly crystallized on addition of absolute ether and was washed with ether and water. The product was purified by reprecipitation from a saturated benzene solution with absolute ether. The compound obtained was insoluble in water and absolute ether, difficultly soluble in cold benzene and readily soluble in methyl and ethyl alcohols and acetone. The m.p. was 184-185°. A chromatogram of the hydrolyzate showed spots of sarcosine, glycine and valine.

Found %: C60.38, 60.15; H 5.45, 5.60; N 11.87, 11.83. $C_{18}H_{19}O_5N_3$. Calculated %: C 60.30; H 5.38; N 11.82.

3. N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride. The acid chloride of N-phthalyl-D,L-norleucine was prepared by the method in [10]. The m.p. was 57-58° (according to literature data: m.p. 59°). From 1.6 g of sarcosyl-D,L-phenylalanine anhydride and 2 g of the acid chloride of phthalyl-D,L-norleucine under the given conditions, we obtained 0.66 g (20%) of N-phthalyl-D,L-norleucyl-sarcosyl-phenylalanine anhydride. The m.p. was 177°. A mixed melting point with phenylalanyl-sarcosine anhydride gave a depression of 30°. The anhydride obtained was insoluble in hot and cold water and absolute ether, but was soluble in methyl alcohol and acetone and with difficulty in ethyl alcohol. A chromatogram of the hydrolyzate showed spots of sarcosine, phenylalanine and norleucine.

Found %: C 67.40, 67.22; H 6.06, 6.05; N 9.18, 9.13. $C_{26}H_{27}O_5N_3$. Calculated %: C 67.68; H 5.86; N 9.11.

4. N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride. 0.5 g (0.003 mole) of glycyl-D,L-valine anhydride and 1.5 g (0.006 mole) of the acid chloride of phthalyl-glycine were ground in a mortar and heated with 20 ml of

absolute xylene at the boiling point of the solvent for 5 hours. After filtration of the solution, the substance was precipitated with absolute ether, the solution evaporated down and carefully washed with water. The product was recrystallized from benzene. The yield was 1.0 g (58%). The m.p. was 195°. The material was soluble in methyl and ethyl alcohols, soluble in benzene on heating and insoluble in ether.

Found %: C 61.21, 61.19; H 4.32, 4.27; N 10.66, 10.68. $C_{27}H_{22}O_8N_4$. Calculated %: C 61.13; H 4.15; N 10.56.

II. Action of 1 Mole of Hydrazine Hydrate in Alcohol on N-Monophthalylaminoacylated sarcosine anhydrides

1. Action of hydrazine hydrate on N-phthalylglycyl-sarcosyl-D,L-valine anhydride. To 0.8 g (0.002 mole) of N-phthalylglycyl-sarcosyl-D,L-valine anhydride was added 2.2 ml of a M solution of hydrazine hydrate in alcohol and 3 ml of ethanol. The mixture was left to stand for 1 hour. We isolated 0.5 g of a substance with m.p. 265°, which reduced copper under the conditions of the biuret reaction. A chromatogram of the hydrolyzate showed one spot – glycine.

According to the analysis data, chromatogram and properties, the substance was phthalylglycyl hydrazide.

Found %: N 20.26, 20.21. $C_{10}H_9O_3N_3$. Calculated %: N 20.17.

The filtrate was concentrated in vacuum and absolute ether added to precipitate 0.21 g of a substance with m.p. 112-114°, which did not depress the melting point of sarcosyl-D,L-valine anhydride. From the melting point and an ascending chromatogram it followed that this compound was sarcosylvaline anhydride (R_f = 0.9).

2. Action of 1 mole of hydrazine hydrate in alcohol on N-phthalyl-D,L-valyl-sarcosyl-glycine anhydride. 1.46 g of N-(phthalyl-D,L-valyl)-sarcosyl-glycine anhydride was heated with 4 ml of a M solution of hydrazine hydrate in alcohol and 12 ml of 96% ethanol. On cooling, the solution deposited 0.03 g of a precipitate, which did not melt at 340° and reduced copper under the conditions of the biuret reaction. A chromatogram of the hydrolyzate, developed with ninhydrin, did not show amino acid spots. The mother liquors yielded a further 0.028 g of the same substance, which was apparently phthalyl hydrazide according to its properties.

Adding water to the alcohol solution gave 0.225 g of a hygroscopic substance, which gave a strong ninhydrin reaction and a blue color in the biuret reaction. It is possible that this substance was D,L-valyl-sarcosyl-glycine anhydride; however an analysis could not be carried out because of the strong hygroscopicity. On a chromatogram in a medium of butanol–water–acetic acid (4 : 5 : 1), there was one spot, different from the starting materials and the decomposition products, which appeared with benzidine and ninhydrin. On an electrochromatogram (ionophoretogram), the D,L-valyl-sarcosyl-glycine anhydride moved 5 cm toward the cathode in an acetic acid buffer over 3 hours with a potential gradient of 6.6 v/cm. A chromatogram of the hydrolyzate gave three spots corresponding to valine, sarcosine and glycine.

III. Absorption Spectra of Copper Complexes of N-Monophthalylaminoacylated Sarcosine Anhydrides

Procedure. 0.01 mole of the substance was dissolved with gentle heating in 9.5 ml of 2 or 4 N NaOH and ¼ M copper acetate solution was added until a large precipitate of copper hydroxide appeared (approximately 0.5 ml). N-Phthalyl-D,L-valyl-sarcosyl-glycine and N-phthalylglycyl-sarcosyl-D,L-valine anhydrides rapidly dissolved in alkali and immediately gave a biuret reaction, whose intensity gradually increased. N-Phthalyl-D,L-norleucyl-sarcosyl-phenylalanine anhydride dissolved with great difficulty in 4 N alkali, even on heating. The intensity of the biuret reaction was very low at first and increased slowly. The results of measuring the absorption spectra maxima are given in Table 3.

In the formation of the copper complex of N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride, a violet color appeared after several minutes and the intensity of this rapidly increased (Table 3).

Isolation of phthaloylglycyl-D,L-valyl-sarcosine from the copper complex. A 0.01 molar solution of biuret copper complex was decomposed by acidification with 10% hydrochloric acid and extracted with benzene, chloroform and ethyl acetate. The extract was dried with calcium chloride and the solvent evaporated to dryness to give a substance which crystallized on standing in a vacuum desiccator. The m.p. was 182°. In the alkaline solution containing copper acetate, a copper complex was formed with an absorption maximum at 640 mμ

(Table 3). The partition coefficient of the substance on an ascending chromatogram with a butanol–water–acetic acid medium, developed with benzidine, corresponded to the N-phthaloylglycyl-D,L-valyl-sarcosine synthesized (R_f = 0.42).

Phthaloylglycyl-D,L-valyl-sarcosine. 1.3 g of the acid chloride of phthalylglycine was dissolved in 10 ml of dioxan and a mixture of 1 g of D,L-valyl-sarcosine and 0.42 g of magnesium oxide in 50 ml of water was added dropwise over a period of 40 minutes with cooling and continuous stirring. The slightly turbid solution was filtered, acidified with hydrochloric acid and evaporated down in vacuum. The needles had m.p. 182°. The substance obtained was soluble in dioxan, chloroform, alcohol and benzene. For purification it was reprecipitated from dioxan with petroleum ether.

Found %: C 54.85, 54.91, H 5.89, 5.90. $C_{18}H_{23}O_7N_3$. Calculated %: C 54.96; H 5.85.

Reaction with copper in an alkaline solution gave a complex with an absorption maximum at 640 mμ, which agreed in the character of the spectrum with that isolated in the decomposition of the copper complex (Table 3).

TABLE 3

Changes in the Absorption Coefficient Maxima of the Decomposition Products of Phthalylaminoacyldiketopiperazines

Name of compound	Change in ϵ_{max} with time											
	0 hours		2 hours		15 hours		54 hours		78 hours		5 days	
	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε
N-Phthalylglycyl-sarcosyl-D,L-valine anhydride	640	0.370	640	0.612	640	0.620	640	0.642	640	0.650	650	0.650
N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride	640	0.315	640	0.530	640	0.545	640	0.550	—	—	—	—
N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride	—	—	—	—	650	0.350	640	0.500	—	—	650	0.512
N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride	560	0.408	560	0.732	560	0.745	580	0.732	580	0.740	—	—
Phthaloylglycyl-D,L-valyl-sarcosine	—	—	650	0.648	does not change							
Phthaloylglycyl-glycyl-D,L-valine	—	—	560	0.738	does not change							

Isolation of phthaloylglycyl-glycyl-D,L-valine from decomposition of the copper complex of N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride. A 0.01 molar solution of the copper complex was decomposed with 10% hydrochloric acid. The substance was extracted with benzene from the acid solution. The benzene was dried with calcium chloride and evaporated in vacuum. The m.p. of the product was 270°. The substance obtained gave a biuret reaction with an absorption maximum at 560 mμ and on an ascending chromatogram in a butanol–water–acetic acid medium (4 : 5 : 1), developed with benzidine, it corresponded to the tripeptide N-phthaloylglycyl-glycyl-D,L-valine (R_f = 0.62) synthesized.

Phthaloylglycyl-glycyl-valine. 1.1 g of phthalylglycyl-glycine was dissolved in 5 ml of dioxan, cooled and 0.12 ml of triethylamine and 0.1 ml of ethyl chlorocarbonate added. A gelatinous precipitate was formed and after cooling for 10 minutes, it was treated with 0.1 g of valine dissolved in 1.5 ml of dioxan and 0.4 ml of 2 N NaOH. After slight shaking, the reaction mixture became clear. To complete the reaction it was left for 12 hours at room temperature and then concentrated under reduced pressure. The oil formed crystallized in a desiccator. The m.p. was 270°. The product was readily soluble in organic solvents. It was reprecipitated from ethanol with petroleum ether.

Found %: C 53.80, 53.84; H 5.50, 5.55. $C_{17}H_{21}O_7N_3$. Calculated %: C 53.82; H 5.54.

SUMMARY

1. The following N-monophthalylaminoacylated derivatives of sarcosine anhydrides were synthesized for the first time: N-phthalylglycyl-sarcosyl-D,L-valine anhydride, N-phthalyl-D,L-valyl-sarcosyl-glycine anhydride and N-phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride.

2. The mixed N,N'-diphthalylaminoacyldiketopiperazine – N,N'-diphthalylglycyl-glycyl-D,L-phenylalanine anhydride – was synthesized for the first time.

3. The absorption spectra of the biuret complexes, prepared from N-phthalylaminoacyldiketopiperazines were measured and the scheme for their decomposition in an alkaline medium was confirmed by the synthesis of phthaloylglycyl-valyl-sarcosine and phthaloylglycyl-glycyl-valine.

4. It was shown that cleavage occurred at the aminoacyl bond when N-monophthalylaminoacyldiketopiperazines were treated with hydrazine hydrate.

Received January 7, 1957

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INVESTIGATION OF PINACOLIN ISOMERIZATION USING LABELED ATOMS

Z. N. Parnes, S. V. Vitt and D. N. Kursanov

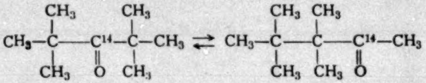
At the present time various investigators have established that aliphatic carbonium ions undergo hydrogen exchange with acids to exchange hydrogen atoms, which are bonded to carbon atoms adjacent to the carbonium center [1-3].

It was also shown [3] that the carbonium center in a carbonium ion, formed by treating a carbonyl compound with sulfuric or another strong mineral acid (at 0°), was incapable of migration, in contrast to the carbonium ion, prepared from a hydrocarbon with a tertiary carbon atom. Thus, on reacting ketones, aldehydes and carboxylic acids with D_2SO_4 or D_3PO_4 only the hydrogen atoms at C_α exchanged.

On the other hand, cases are known of ketone isomerization [4-7] which are explained by the transfer of the carbonium center. Zook and Paviak [6] found that tertiary butyl ethyl ketone (I) when treated with conc. H_2SO_4 for 3 hours at 55° and 2 days at room temperature was 9% converted to tertiary amyl methyl ketone (II).

$$\underset{\text{(I)}}{(CH_3)_3CCOCH_2CH_3} \rightarrow \underset{\text{(II)}}{(CH_3)_3CCH_2COCH_3}$$

Barton and Porter [8] recently proved conclusively that in ketone isomerization the oxygen atom does not transfer from one carbon to another, but that only the hydrocarbon radicals migrate. In order to prove this hypothesis, the authors used ditertiary butyl ketone (III), containing C^{14} in the carbonyl group. It was found that the 2,2,3,3-tetramethylpentanone-4 (IV) obtained by the isomerization contained all the C^{14} in the carbonyl group.

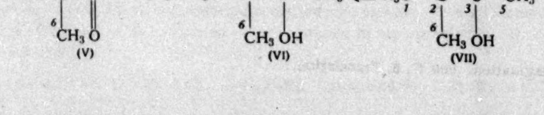


$$\underset{\text{(III)}}{CH_3{-}\overset{CH_3}{\underset{CH_3}{C}}{-}\underset{\overset{\|}{O}}{C^{14}}{-}\overset{CH_3}{\underset{CH_3}{C}}{-}CH_3} \rightleftarrows \underset{\text{(IV)}}{CH_3{-}\overset{CH_3}{\underset{CH_3}{C}}{-}\overset{CH_3}{\underset{CH_3}{C}}{-}\underset{\overset{\|}{O}}{C^{14}}{-}CH_3}$$

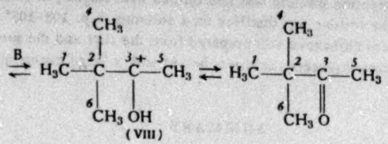
It seemed interesting to us to investigate the reaction of pinacolin (V) with deuterosulfuric acid under the conditions at which the above ketones were isomerized [6].

The assumed isomerization of pinacolin cannot be detected by the usual chemical methods as the reaction product cannot be differentiated from the initial substance; however, one could hope to detect it by using labeled atoms.

According to the data of T. E. Zalesskaia [5] and Barton and Porter, this isomerization should proceed by the following scheme, including the intermediate formation of ion (VII) (asynchronous reaction mechanism).

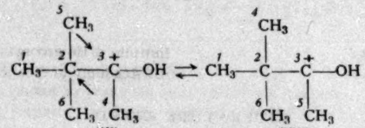


$$\underset{\text{(V)}}{CH_3{-}\overset{CH_3}{\underset{CH_3}{C}}{-}\underset{\overset{\|}{O}}{C}{-}CH_3} \rightleftarrows \underset{\text{(VI)}}{H_3C{-}\overset{CH_3}{\underset{CH_3}{C}}{-}\underset{OH}{\overset{+}{C}}{-}CH_3} \overset{A}{\rightleftarrows} \underset{\text{(VII)}}{H_3C{-}\underset{CH_3}{\overset{+}{C}}{-}\overset{CH_3}{\underset{OH}{C}}{-}CH_3}$$



(VIII)

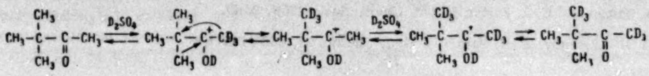
However, on the basis of data we obtained in work on pinacolin rearrangement [9], one can consider that either ion (VII) exists for such a short period that it has no time to enter the hydrogen exchange reaction to any noticeable degree or that it does not form at all and the rearrangement occurs synchronously, i.e., without forming the free ion (VII), as is shown in the scheme below.



(VI) (VIII)

On the contrary, ions (VI) and (VIII) should readily enter the hydrogen exchange reaction. Due to the reversibility of the isomerization, all the hydrogen atoms of pinacolin should be finally exchanged. In this case the trimethylacetic acid, obtained by oxidizing the pinacolin isolated after the reaction, should apparently contain deuterium.

We found that after heating pinacolin with D_2SO_4 at 50° for 10 hours, the tertiary butyl group of pinacolin did not contain deuterium, which indicated the absence of methyl group migration under these conditions. However, after heating at 100° for 11 hours, the pinacolin recovered contained a considerable amount of deuterium in the tertiary butyl group, which corresponded to an exchange of more than three hydrogen atoms. Consequently, under our conditions pinacolin underwent isomerization which, however, due to the similarity of the initial and final substances, cannot be detected readily other than by using labeled atoms.



Synchronous transfer of methyl groups

From the data given above one can assume that hydrogen exchange in this hidden isomerization is the result of the transfer of methyl groups and is not caused by the transfer of the carbonium center.

EXPERIMENTAL

Concentrated D_2SO_4 (19.92 g) (excess density 9050 γ/ml) was gradually added to pinacolin (20.45 g) cooled

Expt. No,	Temp.	Time (in hours)	Excess density of water from combustion (in γ/ml)						
			calculated					experiment	
			semicarbazone			acid		semicarbazone	trimethylacetic acid
			3H	6H	9H	3H	9H		
1	50°	12	7315	—	10030	10970	—	7020	230
2	100	6	7615	9670	—	—	—	10620	—
3	100	11	—	—	—	6675	11760	—	7830

with ice-water. A sealed ampule with the reaction mixture was heated in a thermostat at 100° for 11 hours. At the end of the experiment the reaction mixture was neutralized with Na_2CO_3 or $NaHCO_3$ and extracted with ether. After distillation of the ether, the residue was distilled on a column; b.p. 103-105° (4.7 g). The pinacolin isolated was divided into two parts: a semicarbazone was prepared from the first and the second was oxidized to trimethylacetic acid with NaOBr. The trimethylacetic acid was boiled with a large excess of water, extracted with ether and distilled.

SUMMARY

1. The reaction of pinacolin with deuterosulfuric acid was studied under conditions of ketone isomerization.

It was shown that under these conditions pinacolin exchanged the hydrogen atoms in the tert.-butyl group for deuterium.

2. The reaction mechanism of deuterium exchange and isomerization of pinacolin was examined.

Received January 16, 1957

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the Academy of Sciences USSR

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* Original Russian pagination. See C. B. Translation.

ALKYLATION OF DIPHENYL WITH ALCOHOLS IN THE PRESENCE OF $BF_3 \cdot H_3PO_4$ CATALYST

I. A. Romadan and S. E. Berga

Aromatic hydrocarbons of natural lubricating oils are homologs of benzene, naphthalene and diphenyl. However, individual substances cannot be separated from the natural mixtures. The only substances that can be investigated are synthetic ones, prepared by various methods. Using the method of Ulmann [1], Schreiner [2] prepared p,p'-diethyl-, p,p'-diisopropyl- and p,p'-ditert.-butyldiphenyls. Boedtker [3] synthesized p,p'-ditert.-amyl- and p,p'-di-n-butyldiphenyls by the same method. p-Monoalkyldiphenyls were synthesized by Japanese chemists [4] by the Friedel-Crafts reaction between diphenyl and acid chlorides, with subsequent reduction of the ketones obtained. They prepared p-n-butyl-, p-n-hexyl-, p-n-octyl- and other alkyldiphenyls. The constants are given in the article.

There are few papers on the alkylation of diphenyl. Thus, Grosse, Mavity and Ipatieff [5] alkylated diphenyl with 2,2,4-trimethylpentane in the presence of $AlCl_3 + H_2O$ and obtained p-tert.-butyldiphenyl; Levine and Cass [6] treated diphenyl with propylene and isopropyl chloride using $AlCl_3$ and obtained mono- and diisopropyldiphenyls; Pokrovskaia and Sushchik [7] reacted hexyl bromide with diphenyl using $AlCl_3$. The well-known paper by Nozakura [8] describes the alkylation of diphenyl in the presence of a Japanese clay catalyst. Here, the practical use of higher monoalkyldiphenyls as oils for diffusion pumps is described. The alkylation of diphenyl with alcohols using the catalyst H_3PO_4 [9] has been investigated and diphenyl has been reacted with various alcohols in the presence of BF_3 [10]. In the last two papers, the authors showed that H_3PO_4 directs radicals into the para-position giving mainly monoalkyldiphenyls in yields of up to 60% (calculated on diphenyl). With BF_3 a mixture of mono- and dialkyldiphenyls was obtained with a considerable predominance of the mono derivative. The total yield of the substances obtained was 74-98%, depending on the starting alcohol.

In the present work we examined the reaction between diphenyl, and isoamyl, isobutyl, isopropyl, n-propyl and n-butyl alcohols in the presence of $BF_3 \cdot H_3PO_4$. It was interesting to determine the directing effect of stronger acid catalysts than BF_3 and at the same time to examine the possibility of isomerizing secondary radicals into tertiary ones in the presence of a strong electrophilic reagent. In previous papers [9, 10] we showed that the alkylation of diphenyl with isobutyl alcohol yielded p-tert.-butyldiphenyl with m.p. 52°. In this work we obtained amyldiphenyl with m.p. 46°. Both substances are analogous to alkyldiphenyls, obtained by alkylating diphenyl with tertiary butyl and amyl alcohols. However, the p-tert.-butyldiphenyl, described in the previous paper [9] was, apparently, not quite pure and was therefore characterized as an oily product. Only after careful distillation on a column could we isolate crystalline substances whose molecular weight and elementary composition corresponded to those of monobutyl- and monoamyldiphenyls. When oxidized with nitric acid in sealed tubes, they gave terephthalic acid. The supposed p-tert.-amyldiphenyl reacted slowly with a bromine solution in carbon tetrachloride.

In the work described we again tried to find confirmation for the hypothesis on the mechanism of alkylation with alcohols in relation to structure. Kenne and Sowa [11] and Price and Lund [12] have expressed opinions on the mechanism of alkylation with alcohols in the presence of BF_3. Later, other authors also tried to explain the mechanism of the reaction [13, 14], but concrete hypotheses on the course of the reaction in relation to the alcohol's structure were not, apparently, put forward. Having examined the alkylation of naphthalene [15, 16] and diphenyl [10] with normal and isoalcohols in the presence of BF_3, we can put forward some hypotheses on the alkylation mechanism based on the following facts. 1) Reactions with normal alcohols gave alkylnaphthalenes and diphenyls with only normal radicals; 2) in alkylation with normal alcohols there are no olefin polymerization products; 3) with normal alcohols the reaction proceeded 3-4 times more slowly than with isoalcohols; 4) alkylation with isobutyl and isoamyl alcohols gave alkylnaphthalenes – diphenyls, containing tertiary radicals; 5) in the reactions with isoalcohols the product mixture always contained olefin dimers and trimers; 6) with isoalcohols the reaction was complete in 1-2 hours.

From these observations one may presume that condensation occurs with normal alcohols, while alkylation by intermediate olefins occurs with isoalcohols which split off water more readily.

Name of substance	Boiling point		n_D^{20}	d_4^{20}	Melting point	M	
	at atm. pressure	pressure (in mm)				found	calc.
p-n-Propyldiphenyl	296°	108.4 (0.25)	1.5726	0.9798	1°	193	196
p-p'-Di-n-propyldiphenyl	311	122 (0.2)	1.5570	0.9997	—	—	—
p-n-Butyldiphenyl	299	112 (0.6)	1.5718	0.9684	14	207	210
p-p'-Di-n-butyldiphenyl	317	129 (0.6)	1.5543	0.9622	57	263	266
p-Isopropyldiphenyl	291	103.3(0.34)	1.5692	0.9651	4	200	196
p-Tert.-butyldiphenyl	310	99.3 (01)	—	—	52	208	210
p-p'-Ditert.-butyldiphenyl	326	114.1 (01)	1.5548	0.9502	119	269	266
p-Tert.-amyldiphenyl	300	97 (0.1)	1.5705	0.9671	46	227	224
					Little material		
p-p'-Ditert.-amyldiphenyl	334	124.6 (0.1)	1.5503	0.9479	114	297	294

The same facts are observed in reactions with $BF_3 \cdot H_3PO_4$ catalysts as in the presence of only BF_3: p-n-alkyldiphenyls were obtained with normal alcohols, p-isopropyldiphenyl – with isopropyl alcohol and p-tert.-butyl- and p-tert.-amyldiphenyls (crystalline substances) formed with isobutyl and isoamyl alcohols. Besides monoalkyldiphenyls, dialkyldiphenyls with radicals in the p,p'-positions were obtained. Their yield did not exceed 8-14%. Polymers of isobutylene and isoamylene were also isolated and investigated. Some characteristics of the alkyldiphenyls are given in the table.

EXPERIMENTAL

The catalyst was prepared by saturating orthophosphoric acid (d 1.86-1.87) with dry BF_3 at room temperature. The molecular compound obtained corresponded approximately to the formula $BF_3 \cdot H_3PO_4$.

The alkylation reaction was carried out in a three-necked flask with a mechanical stirrer and a reflux condenser. The catalyst and the diphenyl were placed in the flask and heated to 160° on an oil bath. Alcohol, which had been previously dried and distilled on a column was added dropwise at this temperature. The end of the dropping funnel dipped into the reaction mixture. After the addition of 3 moles of alcohol, the reaction mixture was heated for from 3 to 12 hours, depending on the structure of the alcohol. The BF_3 liberated during the reaction was absorbed in wash bottles with cooled alcohol (usually the same as that used for the reaction). At the end of the evolution of BF_3, the upper layer was separated and treated with superheated steam to remove unreacted diphenyl and olefins. The oil left in the distillation flask was dried and distilled, first over metallic sodium and then on a vacuum column of 48 theoretical plates.

Alkylation of diphenyl with n-propyl alcohol. 154 g of diphenyl, 187 g of n-propyl alcohol (b.p. 98°, $n^{20}D$ 1.3828, $d^{20}{}_4$ 0.8034) and 130 g of catalyst was heated at 160-165° for 12 hours. By distillation over metallic sodium we obtained 192 g of a mixture of propyldiphenyls, which were separated on a vacuum column. Monopropyldiphenyl formed about 90% of the total amount of propyldiphenyls. The total yield was 63% (calculated on the starting diphenyl).

Alkylation of diphenyl with isopropyl alcohol. 1 mole of diphenyl and 3 moles of isopropyl alcohol (b.p. 83°, $n^{20}D$ 1.3965, $d^{20}{}_4$ 0.7883) reacted at 162-165° for 3 hours. p-Isopropyl- and diisopropyldiphenyls were isolated in a total yield of 61%. Propylene polymer with b.p. 100-130° was obtained. It decolorized bromine water and reacted with $KMnO_4$ solution.

Alkylation of diphenyl with n-butyl alcohol. The same ratio of reagents was heated at 165° for 11 hours. Mono- and di-n-butyldiphenyls were obtained in 64% total yield. The mixture of butyldiphenyls had a low solidification point (down to −70°). The p-n-butyldiphenyl, isolated with a vacuum column, had m.p. 14°, which corresponds to the data of Japanese chemists [4], who found m.p. 15.3-16.3° for it. Oxidation of the p-n-butyldiphenyl with an alkaline solution of potassium permanganate (boiling for more than 100 hours) gave p-diphenylcarboxylic acid with m.p. 226° (from alcohol), forming an ethyl ester with m.p. 46° [17]; p,p'-di-n-butyldiphenyl was obtained as an oily substance, from which crystals were isolated with m.p. 57-58° only after the material had stood for 3-4 months. According to Boedtker [3], the m.p. of synthetic p,p'-di-n-butyldiphenyl is 58-59°. The author reported that it was a slowly crystallizing oil and gave the refractive index and the specific gravity. The constants we found were close to those reported by Boedtker.

Alkylation of diphenyl with isobutyl alcohol. 1 mole of diphenyl, 3 moles of isobutyl alcohol (b.p. 108°, $n^{20}D$ 1.3964, d^{20}_4 0.8033) and 0.75 mole of catalyst were heated (160-165°) for 2.5 hours. Distillation on a vacuum column yielded p-tert.-butyldiphenyl with m.p. 52°. A second substance, which had a high boiling point, at first had a solidification point of −17°, but on standing it slowly deposited crystals with m.p. 119° (from alcohol). For p,p'-ditert.-butyldiphenyl, Boedtker reported m.p. 122°. The yield of this substance was 6-8%. It did not react noticeably with bromine at room temperature. The molecular weight and elementary analysis of a third substance corresponded to a monobutyldiphenyl; however it was oily, had a solidification point of −9° and the refractive index and specific gravity were different from those of p-tert.-butyldiphenyl.

Alkylation of diphenyl with isoamyl alcohol. 154 g of diphenyl, 264 g of isoamyl alcohol, carefully distilled on a column, and 130 g of catalyst were heated (160-165°) for 3 hours. We obtained p-tert.-amyldiphenyl (m.p. 46° from anhydrous alcohol). A substance slowly (after standing for 2 months) crystallized from the oily product and had b.p. 310°.

Found %: C 90.02; H 9.93. $C_{20}H_{26}$. Calculated %: C 90.16; H 9.84.

A second substance with b.p. 334° slowly crystallized from methyl alcohol after standing for a month and had m.p. 114°; it reacted with bromine dissolved in CCl_4; the molecular weight and elementary composition corresponded to diamyldiphenyl. Apparently this was p,p'-ditert.-amyldiphenyl, which Boedtker [3] synthesized by Ulmann's method [1]. For it the author reported b.p. 224° (16 mm), $n^{16}D$ 1.5503. We found $n^{20}D$ 1.5503. The yield was 4%.

Found %: C 89.66; H 10.38. $C_{22}H_{30}$. Calculated %: C 89.73; H 10.27.

SUMMARY

1. It was suggested that condensation occurs when diphenyl is heated with normal alcohols and therefore only substances with normal radicals are obtained.

2. With isoalcohols the main reaction is that of alkylation with intermediate olefins and therefore alkylnaphthalenes and alkyldiphenyls containing tertiary radicals are obtained.

3. Alkylation of diphenyl with alcohols in the presence of $BF_3 \cdot H_3PO_4$ required 3 moles of alcohol per mole of hydrocarbon, while alkylation with molecular compounds of alcohols and BF_3 needed only 1.5 moles.

4. The alkyldiphenyl yields were 80-98% in the alkylation of diphenyl with molecular compounds. Reaction with a mixed catalyst however, gave a yield of not more than 65%, although the heating time was increased almost two-fold.

Received January 26, 1957

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** In Russian.

CASES OF HINDERED POLYMERIZATION OF MONOMERS IN THE ARYL METHACRYLATE SERIES

M. M. Koton, T. A. Sokolova, M. H. Savitskaia and T. M. Kiseleva

In studies of the polymerization of aryl methacrylates it has been discovered that some of these, having substituents in the benzene nucleus ortho to the acyl radical, polymerize considerably more slowly than the corresponding para isomers. In order to clarify the problem of the causes of the hindered polymerization of ortho-substituted aryl methacrylates, various such ortho- and para-substituted derivatives were synthesized. If, in these cases, the polymerization process depends on the nature of the substituent, then for example, o- and p-methoxyphenyl methacrylates would polymerize differently from o- and p-nitrophenyl methacrylates because the nitro and methoxy groups are opposite in character. However, it has been shown that in spite of the difference in the nature of the substituents, in both cases the para derivatives polymerize readily and the ortho derivatives with considerably more difficulty (see table). Consequently it is evident that it is the position of the substituent, and not its chemical nature, that determines the behavior of the monomers being compared.

In addition to the methacrylate monomers mentioned above, o- and p-tolyl- and o- and p-diphenyl methacrylates were also synthesized. For the ortho- and para-tolyl methacrylate isomers a quantitative examination of their polymerization was carried out by determination of the percentage conversion by precipitation of the polymer. It was shown that o-tolyl methacrylate did not polymerize at all on heating for 2.5 hours at 80° with 0.3% (by weight) of benzoyl peroxide, whereas the para isomer under identical conditions gave 11.8% conversion. Similarly, a very marked difference was shown also by the diphenylmethacrylate ortho and para isomers.

The proximity of the substituents in the ortho derivatives impedes their polymerization and this can evidently be explained by steric hindrance. The effect on polymerizability of substituting the phenyl by the cyclohexyl radical in the methacrylate molecule was shown by the example of thymol and menthol derivatives.

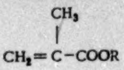
The methacrylate ester of thymol, containing the bulky isopropyl group, polymerizes with difficulty. Evidently steric hindrance is here connected with the coplanar configuration of the benzene ring, which imparts a definite rigidity to the molecule. The methacrylate ester of menthol analogous to this (but having a hydrogenated nucleus in the molecule) polymerizes readily under ordinary conditions. This can be explained by the fact that the carbon atoms in the cyclohexyl ring do not lie in the same plane; consequently the whole molecule of this compound is not rigid like the methacrylate ester of thymol.

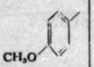
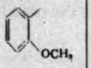
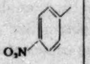
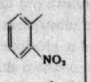
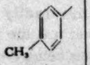
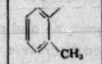
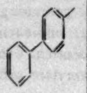
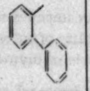
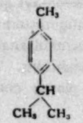
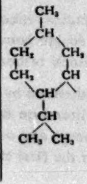
In all these cases hindering of polymerization by a free-radical mechanism can possibly be explained by the screening action of groups that are bulky in relation to the double bond. These groups hinder the addition to the double bond of benzoyl peroxide free radicals, which are also of rather large bulk.

The monomers used in the present investigation were synthesized by methods described in the literature. Their properties are described in the experimental part, where literature data for the compounds described are also quoted for comparison. The p-tolyl, o- and p-methoxy phenyl and o-diphenyl methacrylates as well as the methacrylate esters of thymol and menthol were synthesized for the first time.

EXPERIMENTAL

Preparation of o-methoxyphenyl methacrylate. 37.2 g of guaiacol was dissolved in 200 ml of 5% aqueous sodium hydroxide. 31.5 g of methacrylyl chloride was added from a dropping funnel, with stirring, over a period of 0.5 hours. Stirring was continued for 1 hour at room temperature. The liquid product was then extracted with

Polymerizability of Monomers of the General Structure 
$CH_2{=}C(CH_3){-}COOR$

No.	Monomer	R	Conditions and results of polymerization
1	p-Methoxyphenyl methacrylate		Polymerizes on heating in the presence of 0.3% (by weight) of benzoyl peroxide.
2	o-Methoxyphenyl methacrylate		Does not polymerize with 0.3% benzoyl peroxide. Becomes viscous on further heating for 120 hours at 120°. with 0.5% benzoyl peroxide.
3	p-Nitrophenyl methacrylate		Polymerizes on heating with 0.3% benzoyl peroxide.
4	o-Nitrophenyl methacrylate		Does not polymerize on heating with 0.3% benzoyl peroxide. Polymerizes only with 2% benzoyl peroxide.
5	p-Tolyl methacrylate		Forms 7% of polymer on heating for 2 hours at 80° with 0.3% benzoyl peroxide and 11.8% polymer after 2.5 hours.
6	o-Tolylmethacrylate		Does not polymerize after 2.5 hours heating with 0.3% benzoyl peroxide.
7	p-Diphenyl methacrylate		Polymerizes on heating in the presence of 0.3% benzoyl peroxide.
8	o-Diphenyl methacrylate		Polymerizes with 0.3% benzoyl peroxide only on prolonged heating (about 200 hours) at 120°.
9	Methacrylic ester of thymol		Does not polymerize with 0.3% benzoyl peroxide. Becomes viscous on further heating with 0.5% benzoyl peroxide for a period of 120 hours at 120°.
10	Methacrylic ester of menthol.		Polymerizes with 0.3% benzoyl peroxide under normal conditions.

ether. The extract was washed with alkali solution and water to neutral reaction, dried over anhydrous magnesium sulfate, the ether distilled off, and the residue twice fractionated in vacuo. The o- and p-tolyl and o- and p-diphenyl methacrylates as well as the methacrylate ester of thymol were prepared by the same method.

Preparation of the methacrylate ester of menthol. 15.6 g of menthol was placed in a round-bottomed flask fitted with a mechanical stirrer and reflux condenser; the menthol was melted, and 12 g of methacrylyl chloride was added with stirring and heating to 80°; after the addition, heating at 80° was continued for 3 hours. The liquid product was extracted with ether. The extract was washed with a 5% solution of sodium hydroxide, and subsequently with water, to neutral reaction. The ether was distilled from the extract after drying over anhydrous magnesium sulfate and the residue fractionated in vacuo. p-Methoxy phenyl methacrylate was prepared in the same way.

Preparation of o-nitrophenyl methacrylate. A mixture of 1 mole of o-nitrophenol and 2 moles of methacrylyl chloride was heated for 2 hours in pyridine, in a flask with a reflux condenser, at the boiling point of the mixture. The mass, solidified by cooling, was washed with water to remove pyridine and the residual oil, after washing with sodium hydroxide solution and water, and drying, was distilled in vacuo.

p-Nitrophenyl methacrylate was prepared in the same way.

Properties of the Monomers

o-Methoxyphenyl methacrylate is a colorless oil, which redistils at 109-110° at 4 mm. Yield 51%, $n^{25}D$ 1.5235.

Found %: C 68.67; H 6.53. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

p-Methoxyphenyl methacrylate crystallizes in the form of colorless plates, m.p. 63-64°. Yield 53%.

Found %: C 68.58; H 6.25. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

p-Tolyl methacrylate. Colorless liquid, b.p. 103° at 7 mm. Yield 72%, d^{20}_4 1.025, $n^{20}D$ 1.5135.

o-Diphenyl methacrylate. Colorless liquid, b.p. 144-145° at 4 mm. Yield 50%, d^{20}_4 1.107, $n^{20}D$ 1.5897.

Found %: C 80.56; H 6.17. $C_{16}H_{14}O_2$. Calculated %: C 80.67; H 5.88.

Methacrylic ester of thymol. Colorless liquid with an aromatic odor. B.p. 127° at 10 mm. Yield 53%, $n^{22}D$ 1.5070.

Found %: C 77.13; H 8.33. $C_{14}H_{18}O_2$. Calculated %: C 77.06; H 8.25.

Methacrylic ester of menthol. Colorless liquid, b.p. 107-108° at 6 mm. Yield 68.1%, $n^{17}D$ 1.4025.

Found %: C 75.11; H 10.95. $C_{14}H_{24}O_2$. Calculated %: C 75.0; H 10.71.

o-Tolyl methacrylate. Colorless liquid, b.p. 99° at 7 mm. Yield 67.6%, d^{20}_4 1.034, $n^{18}D$ 1.5112, (according to literature data [1] b.p. 98-103° at 5 mm, d^{20}_4 1.031, $n^{18}D$ 1.5160).

p-Diphenyl methacrylate. Colorless crystals, m.p. 111-112° (according to the data of [1], m.p. 110°).

o-Nitrophenyl methacrylate. Oily, yellow liquid, b.p. 138-139° at 5 mm. Yield 46.1% (according to the data of [2], b.p. 134-136° at 2 mm).

p-Nitrophenyl methacrylate. Colorless needles, m.p. 95° (according to the data of [2], m.p. 93-94°). Yield 60%.

Polymerization of the Monomers

Polymerization of the methacrylates under investigation was carried out in bulk, under identical conditions. Where there were any variations these are indicated in the table. A weighed sample of about 2 g of monomer was placed in a glass ampoule, to which was added 0.3% (by weight) of initiator (benzoyl peroxide). The ampoule, cooled in solid carbon dioxide, was sealed in an atmosphere of air. Heating of the ampoule was carried out in a thermostat. Starting at 70° the temperature was raised every 24 hours to 80, 100 and 120°. Exception was made for those monomers with melting points above 70°. In these cases, heating was commenced a few degrees above the melting point in order to ensure homogeneity of the medium. The end point of polymerization was decided by the deposition of polymer on the glass.

SUMMARY

1. It has been shown that ortho-substituted aryl methacrylates display hindered polymerization in comparison with their para isomers.

2. This hindered polymerization can be explained by steric hindrance in the monomer molecule.

3. The polymerizability of ortho-substituted methacrylates increases markedly in changing from the coplanar aromatic radical to the corresponding, noncoplanar cycloparaffin radical.

4. The methacrylate esters of p-cresol, guaiacol, p-methoxyphenol, o-hydroxydiphenyl, thymol and menthol, not previously described in the literature, have been synthesized and characterized.

Received January 11, 1957

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*Original Russian pagination. See C. B. Translation.

THE STRUCTURE OF THE POTASSIUM-DIVINYL (BUTADIENE) POLYMER

A. I. Iakubchik and N. N. Motovilova

The dependence of the properties of the polymer and its content of external double bonds* on the nature of the alkali metal used as polymerization initiator, and on reaction temperature, has been established by a number of investigators [1]. In the present work it was proposed to examine the effect of the degree of polymerization on the content of 1,2 linkages in the polymers and on some of their properties (glass temperature, coefficient of freeze-resistance). The polymer obtained by the polymerization of gaseous butadiene by the action of potassium, was chosen as the material to be investigated for the solution of this problem. This polymer is different in many respects from SKB rubber, produced by the polymerization of butadiene in the presence of sodium.

Ozonolysis, first used by Harries in the study of the structure of various rubbers [2], was chosen as the method of investigation, and also a method based on the different rates of oxidation of the internal and external double bonds in the polymer, by benzoyl hydroperoxide (perbenzoic acid) [3-6]. The determination of the polymer structure by the ozonolysis method depended on a single, specific, structural characteristic, namely on the content of 1,2 linkages, that form formic acid and formaldehyde in the final stage of ozonolysis. For the determination of formic acid the method of Fincke [7], based on the reduction of mercuric to mercurous chloride, was used; for the determination of formaldehyde the method of Fosse [8], based on the formation of the condensation product of formaldehyde with β-naphthol, has been acknowledged to be the most suitable, giving more reproducible results than other methods proposed for this purpose.

TABLE 1

No. of sample	Increment of polymer (g. per 1 g. metal)	Proportion of 1,2 segments (%)	Glass temp.	Coefficient of freeze-resistance of vulcanizate
1	160	62.0	—	0.30
2	255	60.0	−60.5°	0.36
3	—	64.8	−59.0	0.27
4	515	58.4	−61.0	0.43
5	765	57.2	−62.0	0.43
6	1000	59.0	−61.0	0.30
7	1520	55.8	−62.0	0.43
8	2000	54.0	−63.5	0.48

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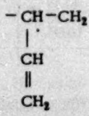
* The grouping  $-\underset{\underset{CH_2}{\overset{\|}{CH}}}{\overset{}{CH}}-CH_2-$, formed by combination of butadiene molecules in the 1,2 position, are called segments with external double bonds; segments with internal double bonds $-CH_2-CH=CH-CH_2-$ are formed by combination in the 1, 4 position.

For the determination of total unsaturation, which is necessary for the quantitative determination of 1,2 and 1,4 segments in the polymer, use was made of the reaction with iodine monobromide which, as A. A. Vasil'ev [9] has shown, gives more reliable results than the reaction with iodine monochloride, normally used. In order to be able to calculate the percentage of the carbon skeleton occurring in 1,2 polymer segments, elementary analysis of the polymer samples was carried out, which also allows the extent of oxidizability of the polymer (purified) to be determined. Polymers obtained at different degrees of polymerization, measured by the so-called "increment," i.e., the quantity of polymer per 1 g of metal, were investigated. The results obtained are given in Table 1.

The data presented indicate a tendency to some degree of lowering of the content of 1,2 segments, which is confirmed by a parallel lowering in the glass temperature of the polymer and an increase in the coefficient of freeze-resistance of its vulcanizate. The reduction in the content of segments with external double bonds could be explained by isomerization of such segments during the polymerization process or during ozonolysis, which has been established by a number of investigators [10-12]. Another explanation might be an increase in the actual polymerization temperature resulting from deterioration of the heat-removal conditions with increasing "increment" of polymer; the latter explanation is the most probable and is confirmed by the small increase in content of 1,4 segments found in the polymer.

EXPERIMENTAL

The initial polymer was obtained by passing gaseous butadiene at 10° (in a bath) over a 5% dispersion of potassium in paraffin, placed in flasks on a framework. Polymerization was carried out simultaneously in eight flasks and was interrupted after the attainment of a chosen "increment," determined by weighing. Thus 8 samples of polymer were obtained with increments varying between 150 and 2000. In order to prevent the possibility of oxidation the samples were treated with 2% Neozon D. Purification of the polymer was carried out by reprecipitation by alcohol from benzene solution with subsequent drying to constant weight at 30°, in vacuo. The samples were stored in sealed tubes, filled with purified nitrogen.

Ozonolysis was carried out in ~1% chloroform solution with a constant ozone concentration in the gas (3-4%) obtained by maintaining a constant gas flow (20 liters per hour) and keeping a constant voltage on the transformer winding of 95-100 v. The method of ozonolysis was the same as that described earlier [13]. After completion of ozonolysis the chloroform was distilled off in vacuo, the ozonide dissolved in ether and kept in ether for a period of 15-20 hours. After the ether was distilled off, the ozonide was dried to constant weight and decomposed by heating with a 10-fold quantity of water. The resulting aqueous solution was transferred to a measuring flask from which test portions were removed for determination of formaldehyde. Results of these determinations are given in Table 2.

TABLE 2

No. of sample	Weight of precipitate Hg_2Cl_2 (in g)	Weight of formic acid in ozonide decomposition products	Carbon content of formic acid obtained (in g)	Weight (in g)		
				Dihydroxydinaphthylmethane precipitate*	Formaldehyde in ozonide dec'mp products	Carbon content of formaldehyde obtained
1	0.7461	0.7265	0.1889	0.00181	0.181	0.0724
2	0.8026	0.7826	0.2035	0.00110	0.110	0.0440
3	0.7148	0.6964	0.1931	0.00176	0.176	0.0704
4	0.6890	0.6718	0.1746	0.00134	0.134	0.0536
5	0.6152	0.5998	0.1559	0.00108	0.108	0.0432
6	0.5597	0.5457	0.1419	0.00154	0.154	0.0616
	0.6961	0.6787	0.1765	0.00109	0.109	0.0436
7	0.6953	0.6779	0.1762	0.00118	0.118	0.0472
	0.6906	0.6729	0.1750	0.00093	0.093	0.0376
8	0.5679	0.5437	0.1414	0.00091	0.091	0.0364

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* After recalculation to 10 g of solution of ozonolysis products.

Determination of the content of 1,2 segments on the basis of the data obtained was carried out by the method described in an earlier paper [13]. The data obtained are given in Table 3.

TABLE 3

No. of sample	Results of elementary analysis** (in %)		Weight of carbon		% carbon skeleton found in formic acid and formaldehyde	Content of 1,2 segments in the rubber (%)
	C	H	In formic acid and formaldehyde	In sample taken for ozonolysis		
1	87.91	11.66	0.2613	1.68	15.5	62.0
2	88.58	11.45	0.2475	1.65	15.0	60.0
3***	88.34	11.46	0.2515	1.55	16.2	64.8
4	87.45	11.22	0.2282	1.56	14.6	58.4
5	88.61	11.30	0.1831	1.28	14.3	57.2
6	88.12	11.57	0.1854	1.29	14.75	59.0
7	88.11	11.53	0.2380 0.2234 0.2122	1.56 1.56 1.56	13.95	55.8
8	87.80	11.31	0.1758	1.31	13.5	54.0

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* Mean of two determinations. Calculated for butadiene polymer: C 88.88; H 11.11.

** Increment figure unknown.

In using the method of oxdiation of the polymer with benzoyl hydroperoxide (perbenzoic acid) it was intended only to obtain the oxidation curves and compare them with the oxidation curves of the dimer of butadiene (vinyl--1-cyclohexene-3), with the object of clarifying the question of whether any change in the amount of internal double bonds, which serves as a measure of the initial combination of butadiene molecules in the 1,4 position, takes place during the polymerization process. Oxidation of the internal double bonds in the polymer was considered to be complete when in a parallel experiment on the oxidation of the dimer the reaction reached 50%, which corresponds to oxidation of all the internal double bonds. Although the method in this form cannot be considered sufficiently accurate, nevertheless it is possible to decide approximately that the proportion of 1,4 segments is about 40%, there being some increase depending on the depth of polymerization. Thus,for example, for samples 1,4 and 7, with the same degree of oxidation of the dimer (51%), the following figures were obtained for the content of 1,4 segments: 41.8, 42.2 and 44.8%. On determination of the total unsaturation by reaction with iodine monobromide, values were obtained (for purified polymer) fluctuating between the limits 90.0 and 91.9%, no systematic variation with depth of polymerization being observed.

SUMMARY

1. The content of segments with external double bonds in potassium-butadiene polymer, determined by the ozonolysis method, decreases to some extent with increasing depth of polymerization. The values of the glass temperature of the polymer and of the coefficient of freeze resistance of the vulcanizate change correspondingly.

2. The number of segments with internal double bonds, determined by oxidation with benzoyl hydroperoxide (perbenzoic acid), remains practically constant; the data obtained are not sufficiently accurate to draw rigid quantitative conclusions.

3. The unsaturation of the polymer, determined by reaction with iodine monobromide, remains constant.

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Received January 14, 1957

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Synthetic Rubber

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* In Russian

INVESTIGATIONS ON CONJUGATED SYSTEMS

LXXXIII. THE STRUCTURE AND REACTIVITY OF THE METHYL ESTER OF VINYLACETYLENE CARBOXYLIC ACID

A. A. Petrov, K. B. Rall and G. I. Semenov

In connection with the systematic investigations that we had undertaken on addition reactions of compounds with double and triple bonds, we were interested in the reactivity of vinylacetylene carboxylic acid and its derivatives. Vinylacetylene carboxylic acid was synthesized as far back as 1938, but the pure acid had not been isolated in the pure form. At the same time its esters were found to possess adequate stability: they have been isolated in the pure form and characterized [1]. Addition reactions of vinylacetylene carboxylic acid and its esters have not been studied.

We prepared the methyl ester of vinylacetylene carboxylic acid by the previously described method and investigated its reaction with bromine. The experiments showed that addition of bromine is very slow and is accelerated by light (Fig. 1). The resultant dibromide changes appreciably when distilled in vacuo (5 mm); we therefore decided to determine its structure with the help of the infrared spectrum without isolating it from the solution in CCl_4 in which the bromination was effected. It was earlier shown that the infrared spectra of dibromides of vinylacetylenic compounds enable precise determination of their structure [2, 3].

The infrared spectrum of the original methyl ester of vinylacetylene carboxylic acid was plotted in advance. This was necessary for evaluation of the structure of the dibromide and there were no data in the literature.

For the purpose of comparison, the spectra of the methyl ester of propiolic acid and of the dimethyl ester of acetylene dicarboxylic acid were plotted under the same conditions. The literature contains details of the vibrational spectra of these esters [4, 5].

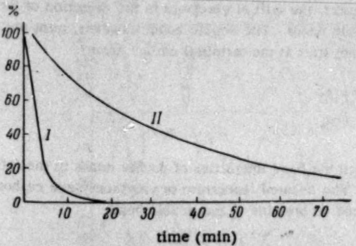


Fig. 1. Rate of bromination of vinylacetylene carboxylic ester in the dark (II) and in diffused light (I).

In the range of frequencies corresponding to the valence CH vibrations the infrared spectrum of the methyl ester of vinylacetylene carboxylic acid contains six bands. Three of these belong to the methyl radical, possibly with superposition of other frequencies (2976, 2907 and 2849 cm^{-1}). These bands are also present in the spectra of the methyl esters of propiolic and acetylene dicarboxylic acids, as well as in the spectra of methanol and dimethyl ether[6]. The other two bands are characteristic of compounds containing the vinyl group (3135 and 3049 cm^{-1}) [7]. Both of these frequencies are also present, however, in the spectra of the methyl esters of propiolic and acetylene dicarboxylic acids which of course do not contain vinyl groups. The frequency of about 3400 cm^{-1} is developed in the spectra of acetylenic aldehydes and ketones and is absent from the spectra of vinylacetylenic hydrocarbons [7, 8]. We assume that this is an overtone (1700 × 2).

The ester of propiolic acid absorbs strongly at 3280 cm^{-1} (ν_{CH} of the terminal acetylenic group).

In the region of frequencies of the deformation CH vibrations the spectrum of vinylacetylene carboxylic acid contains two frequencies (1447 and 1272 cm^{-1}). A frequency of 1414 cm^{-1} is characteristic of the vinyl group. Here this frequency is not differentiated. The 1272 cm^{-1} frequency is very strong, probably due to superposition of several frequencies.

The nonplanar CH vibrations are represented by a pair of frequencies characteristic of the vinyl group (945 and 973 cm^{-1}). The lower frequency has a value slightly higher than in the spectra of hydrocarbons. Acetylene dicarboxylic acid ester does not absorb in this region. Propiolic ester has an intense band at 992 cm^{-1} which is also represented in the spectra of α,β-unsaturated acetylenic aldehydes and ketones. This is probably caused by the CC vibrations at the bond between the carbonyl and the acetylenic grouping.

The strong 2247 cm^{-1} band corresponds to the triple bond. Vinylacetylenic hydrocarbons are characterized by a higher frequency [7] and acetylenic aldehydes and ketones [8, 9] as well as the nearest homolog of vinylacetylene carboxylic ester [5] by a lower frequency of the triple bond. The acetylenic bond also corresponds to a higher value of $\nu_{C\equiv C}$ in the spectrum of propiolic acid ester than in the spectra of acetylenic aldehydes and ketones. No absorption occurs in the spectrum of acetylene dicarboxylic acid ester due to the symmetry of the molecule in the region where the bands characteristic of disubstituted acetylenes are usually observed.

In the spectrum of the methyl ester of vinylacetylene carboxylic acid the double bond is represented by the strong 1608 cm^{-1} frequency. The same frequency was found in the spectra of vinylalkylacetylenes [7].

All of the three esters that were compared have an extremely intense $\nu_{C=O}$ absorption band at 1730 cm^{-1}. According to the literature propiolic and acetylene dicarboxylic acid esters absorb at 1720 cm^{-1} [5].

The ester grouping is evidently associated in all of the spectra with bands in the 1120-1200 cm^{-1} region.

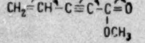
All of the spectra are rich in frequencies of low and medium intensity (probably overtones and proper frequencies).

The spectrum of the dibromide of vinylacetylene carboxylic ester differs from the spectrum of the original ester in being free of appreciable absorption in the 1600 cm^{-1} region and in containing only one band in the 900--1000 cm^{-1} region. Consequently the dibromide no longer contains the vinyl group.

No appreciable increase of absorption occurred in the 1950 cm^{-1} region, which is evidence of the absence of appreciable quantities of the allenic dibromide from the solution.

At the same time the absorption band of the acetylenic grouping was, as before, extremely stong. It has therefore been established that the dibromide of the methyl ester of vinylacetylene carboxylic acid is an acetylenic compound. Consequently addition of bromine took place at the double bond, i.e., in the same manner as in vinylacetylenic hydrocarbons of analogous structure – vinylalkylacetylenes [10].

In the molecule of vinylacetylene carboxylic acid ester, the shift of electrons in the direction of the carbonyl group strongly reduces the reactivity of the double and triple bonds. The double bond, however, turns out to be more reactive to bromine, and the attack evidently does not start at the terminal carbon atom.



$$CH_2{=}CH{-}C{\equiv}C{-}\underset{\displaystyle OCH_3}{\underset{|}{C}}{=}O$$

A certain relation was previously established between the band intensities of double bonds in the infrared spectra and the reactivity of a system of these bonds [7]. The infrared spectrum of vinylacetylene carboxylic ester is similar to the spectra of those hydrocarbons that add on bromine at the double bond.

EXPERIMENTAL

Vinylacetylene carboxylic acid was prepared by the action of carbon dioxide on vinylacetylene magnesium bromide. Its methyl ester was prepared by the procedure of I. N. Nazarov and M. V. Kuvarzina [1]. The two other esters were prepared from the corresponding acids and methyl alcohol under the action of sulfuric acid in the cold. The constants of all of the esters agreed with the literature data.

Principal Absorption Bands in the Infrared Spectra

Methyl ester				Methyl ester			
of propiolic acid	of vinylacetylene carboxylic acid	acetylene dicarboxylic acid	Dibromide I	of propiolic acid	of vinylacetylene carboxylic acid	acetylene dicarboxylic acid	Dibromide (I)
3401 m	3401 m	3401 m	3378 w	**1730** vs	**1730** vs	**1730** vs	**1730** vs
3279 s	—	—	—	—	**1608** s	1634^{+} s	—
3106^{+} m	3135^{+} m	3175^{+} m	—	1560^{+} m	—	—	—
3049 s	3049 s	3030 s	3003 m	1522^{+} m	1508^{+} m	1499^{+} s	—
3021 s	—	—	—	1441 s	1447 s	1441 s	1441 s
2976 s	2976 s	2976 s	2941 s	—	—	—	1377 m
2907^{+} m	2907^{+} s	2899^{+} m	—	—	—	—	1326 s
2825 m	2849^{+} s	2833 m	2817 m	1263 s	1272 vs	1269 vs	1280 s
2710 w	—	2762^{+} w	—	1232^{+} s	1199 s	—	1172—1248 s
2646 w	2660 w	2618 w	—	1131 s	1124 s	1126^{+} s	1121 s
2571 w	—	2551 w	—	1080 m	—	—	—
—	2513 w	2494 w	2494 vw	1040 m	1046 s	1046 s	1038 s
2427 m	2457 vw	2375 w	2392 vw	992 s	—	—	—
2320 w	2364^{+} w	2326 w	—	—	**976** vs	—	—
2304 w	2304^{+} m	—	—	—	**945** vs	—	954 m
—	**2247** vs	—	**2260** s	858 s	—	895 s	885 m
2137 s	2151^{+} w	2160 m	2146 vw	—	804 s	826 s	—
—	—	2114 m	—	765 s	776^{+} m	761 s	—
—	2062 m	2012 m	2062 m	723—707 m	749 s	—	—
1980 m	1961 m	1942 w	1965 w	—	695 m	—	694 w
—	1908 m	1980^{+} m	—				

Note. The plus sign denotes frequencies appearing as superpositions on other, more differentiated frequencies. s = strong, m = medium, vs = very strong, w = weak, vw = very weak.

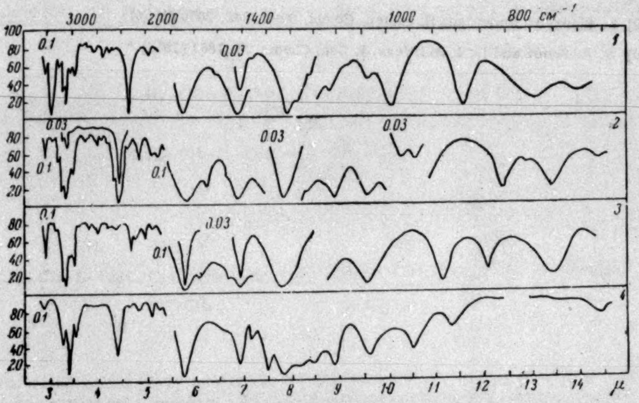


Fig. 2. Infrared transmission spectra. 1) Methyl propiolate; 2) methyl ester of vinylacetylene carboxylic acid; 3) dimethyl ester of acetylene dicarboxylic acid; 4) dibromide of methyl ester of vinylacetylene carboxylic acid.

Infrared spectra were obtained with the IKS-2 spectrometer with an LiF prism in the range up to 5.5 μ and afterwards with an NaCl prism. The spectrum of the dibromide of vinylacetylene carboxylic ester was taken in CCl_4 in comparison with this solvent. Data are presented in the table and Fig. 2.

The rate of bromination of vinylacetylene carboxylic acid ester was investigated in 1% chloroform solution at 22° in the dark and in diffuse light. An equimolar quantity of bromine was taken. The curve of change of concentration of bromine with time is plotted in Fig. 1. The sequence of addition of bromine (judging by the infrared spectrum) is the same in the dark and in the light.

SUMMARY

1. The reaction of the methyl ester of vinylacetylene carboxylic acid with bromine was investigated.

2. On the basis of comparison of the infrared spectra of the dibromide and the original compound, it was shown that the reaction goes preferentially at the double bond.

3. Some of the main regularities in the infrared spectrum of the methyl ester of vinylacetylene carboxylic acid were analyzed.

Received February 20, 1957

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* Original Russian pagination. See C. B. translation.

OXIDATION OF VINYLACETYLENIC HYDROCARBONS BY ORGANIC HYDROPEROXIDES

V. OXIDATION OF 6,9-DIMETHYL-5,9-TETRADECADIEN-7-YNE, 4,7-DIMETHYL-3,7-DECADIEN-5-YNE AND 3,6-DIETHYL-2,6-OCTADIEN-4-YNE BY ACETYL HYDROPEROXIDE

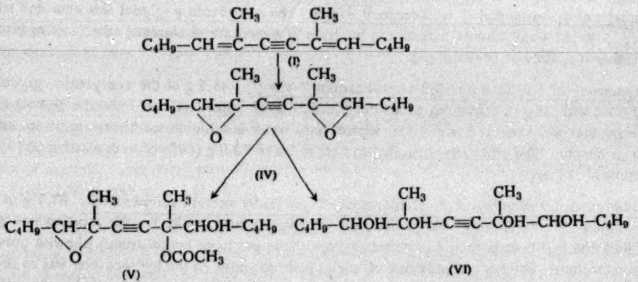
N. M. Malenok, S. D. Kul'kina and Z. Iu. Kovtunenko

In the oxidation by acetyl hydroperoxide of divinylacetylenic hydrocarbons containing the olefinic bonds in the α-position to the triple bond, $-\overset{|}{C}=\overset{|}{C}-C\equiv C-\overset{|}{C}=\overset{|}{C}-$, dioxides are formed but the triple bond remains intact and its presence is confirmed by bromination.

For further confirmation of this fact, previously established by us [1], we subjected three divinylacetylenic hydrocarbons to oxidation: 6,9-dimethyl-5,9-tetradecadien-7-yne (I), 4,7-dimethyl-3,7-decadien-5-yne (II) and 3,6-diethyl-2,6-octadien-4-yne (III). These hydrocarbons were prepared by dehydration of the corresponding γ-acetylenic glycols.

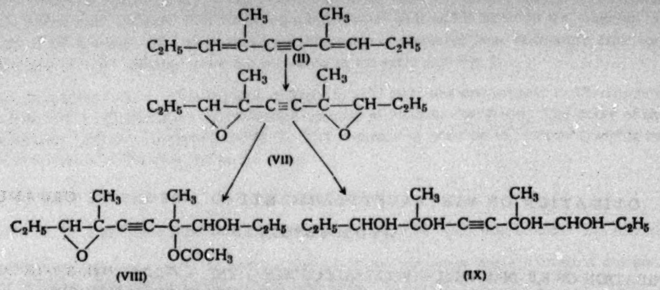
Oxidation of hydrocarbon (I) by acetyl hydroperoxide gave us 6,9-dimethyl-5,9-diepoxy-7-tetradecyne (IV) as the main product, together with the monohydroxide – 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn-10-ol (V) which is a secondary product resulting from reaction of the dioxide (IV) with acetic acid. This is confirmed by the fact that acetylene dioxides directly form monoxides – alcohol-acetates [2] – on heating with glacial acetic acid.

Hydrolysis of (IV) with 1% sulfuric acid gave the erythritol, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol (VI).

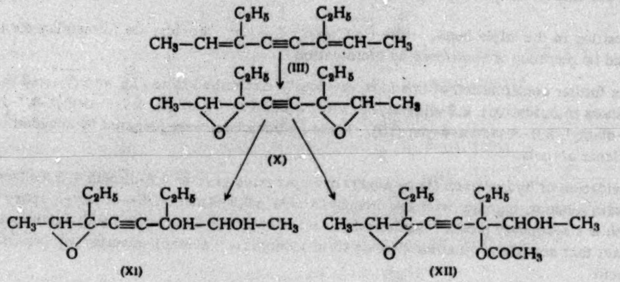


Oxidation of hydrocarbon (II) by acetyl hydroperoxide gave two substances: a dioxide – 4,7-dimethyl-3,7-diepoxy-5-decyne (VII) – and a monoxide – 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol (VIII). The latter is likewise a secondary reaction product resulting from the reaction of the dioxide (VII) with acetic acid.

Hydrolysis of dioxide (VII) gives the erythritol, 4,7-dimethyl-5-decyn-3,4,7,8-tetralol (IX).



Oxidation of the dienynic hydrocarbon (III) by acetyl hydroperoxide gave three substances: a dioxide, 3,6-diethyl-2,6-diepoxy-4-octyne (X); a monoxide, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol (XI); and another monoxide, 3,6-diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol (XII). The last two substances (XI and XII) are secondary products resulting from reaction of the dioxide (X) with water and with acetic acid:



EXPERIMENTAL

Synthesis of 6,9-dimethyl-7-tetradecyn-6,9-diol. The acetylenic γ-glycol was obtained from methyl amyl ketone (b.p. 148-151°) and ethynyl magnesium bromide in a medium of absolute ether. After recrystallization from methyl alcohol it melted at 86-86.5° [3].

Preparation of 6,9-dimethyl-5,9-tetradecadien-7-yne (I). 45.5 g of the acetylenic glycol was heated in vacuo (30 mm) with 18 g of anhydrous potassium bisulfate until water (split off from the glycol) ceased to distil over. The product was extracted with ether, washed with water and sodium carbonate solution, and dried with potassium carbonate. The ether was then distilled off to leave 38.9 g (80%) of hydrocarbon (I) [3] with b.p. 111--115° (2 mm) $n^{20}D$ 1.4855.

Oxidation of 6,9-dimethyl-5,9-tetradecadien-7-yne (I) by acetyl hydroperoxide. 87.7 g of hydrocarbon dissolved in anhydrous ethyl ether was placed in a freezing mixture (−8°). To the solution was gradually added 77.1 g of 80.5% acetyl hydroperoxide (2 moles hydroperoxide per mole hydrocarbon) likewise previously diluted with anhydrous ether. The rate of addition of acetyl hydroperoxide to the hydrocarbon was so regulated that the temperature of the reaction mixture did not rise above −3°. After the whole of the hydroperoxide had been added, the mixture was stood at room temperature.

The progress of oxidation was followed by titration of the reaction mixture and checking of the experiment with 0.1 N thiosulfate solution. For this purpose, 20 ml each of experimental solution (previously diluted 100 times with water) and test solution were taken, and the amount of unreacted acetyl hydroperoxide was determined iodometrically. Results are presented in Table 1 which shows that the oxidation of 6,9-dimethyl-5,9-tetradecadien-

-7-yne (I) by acetyl hydroperoxide proceeded over a period of 9 days. The concentration of hydroperoxide in the control experiment after this period changed to an insignificant extent (Table 1).

TABLE 1

Type of experiment	Amount of 0.1 N thiosulfate consumed in titration of unreacted acetyl hydroperoxide (in ml)									
	Days									
	1	2	3	4	5	6	7	8	9	10
Main	7.30	1.65	1.25	1.00	0.80	0.70	0.60	0.55	0.40	0.40
Control	7.30	7.30	7.30	7.30	7.30	7.20	7.20	7.20	7.20	7.20

After 10 days the reaction mixture was neutralized with 10% sodium carbonate solution and washed once with water. The ether layer was collected and dried with sodium sulfate; the ether was driven off and the residue fractionally distilled three times to give two substances: 1) b.p. 116-117° (0.5 mm), 36 g; 2) b.p. 160-164° (0.5 mm), 3 g.

The substance with b.p. 116-117° (0.5 mm) is a greenish-yellow liquid, soluble in organic solvents, insoluble in water. It slowly releases iodine from an acidified aqueous solution of potassium iodide, slowly decolorizes a chloroform solution of bromine, does not give a reaction for active hydrogen with methyl magnesium iodide, and gives a negative reaction for the ketone group.

$n^{20}D$ 1.4578, d^{20}_{20} 0.9098, MR_D 74.95; calc. 74.37.

Found %: C 76.51, 76.44; H 10.37, 10.49. M 236.5. $C_{16}H_{26}O_2$. Calculated %: C 76.80; H 10.40. M 250.

The substance is the dioxide, 6,9-dimethyl-5,9-epoxy-7-tetradecyne (IV).

The compound with b.p. 160-164° (0.5 mm), $n^{20}D$ 1.4809 is a very viscous, poorly mobile liquid, soluble in the same solvents as the dioxide.

Found %: C 70.79, 70.63; H 9.97, 10.07. M 322. $C_{18}H_{30}O_4$. Calculated %: C 69.68; H 9.68. M 310.

The compound analyzed is the monoxy-alcohol-acetate, 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn-10-ol (V). The analytical data indicate that this compound is insufficiently pure; it is evidently contaminated with dioxide.

Hydrolysis of 6,9-dimethyl-5,9-diepoxy-7-tetradecyne (IV). 4.7 g of the dioxide was boiled for 4 hours (frequent vigorous stirring) with 35 ml of 1% H_2SO_4. The upper layer thickened. The aqueous acidic layer was separated; the viscous layer was dissolved in ether and at the same time the ether-insoluble erythritol came down in the form of crystals. The latter were filtered, washed with ether 3 times and recrystallized from 40% ethyl alcohol. Yield 0.97 g with m.p. 193-194°.

Found %: C 67.06, 66.97; H 10.51, 10.85. $C_{16}H_{30}O_4$. Calculated %: C 67.13; H 10.48.

The erythritol, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol (VI), is readily soluble in methyl and ethyl alcohols, insoluble in water, benzene and ethyl ether. The number of hydroxyl groups and the molecular weight could not be determined due to its insolubility in the solvents usually employed for these determinations.

Synthesis of 4,7-dimethyl-5-decyn-4,7-diol. The acetylenic γ-glycol was prepared from methyl propyl ketone (b.p. 102-103° at 756 mm) and ethynyl magnesium bromide. M.p. 59° [4].

Dehydration of 4,7-dimethyl-5-decyn-4,7-diol by potassium bisulfate. To 58 g of fused γ-glycol was added 25 g of anhydrous $KHSO_4$. Heating in vacuo (40 mm) led to removal of water which was distilled off for 30 minutes. The reaction product was extracted with ether and dried with calcium chloride. A second fractional distillation gave 32 g of a light-yellow liquid, soluble in common organic solvents and corresponding to the divinylacetylenic hydrocarbon, 4,7-dimethyl-3,7-decadien-5-yne (II) [4].

B.p. 72-74° (0.5 mm), n^{20}D 1.4878, d$^{20}_{20}$ 0.8155.

Oxidation of 4,7-dimethyl-3,7-decadien-5-yne (II) by acetyl hydroperoxide. 32 g of the hydrocarbon was oxidized in a medium of anhydrous ethyl ether with 42 g of acetyl hydroperoxide (72%) (2 moles of hydroperoxide to 1 mole of hydrocarbon) at 0°. The temperature of the reaction mixture rose to +5°. Iodometric analysis showed that oxidation of the hydrocarbon proceeded for 8 days. Reaction products were isolated under the same conditions as in the first preparation. Two substances were obtained: 1) b.p. 87.5-88° (0.5 mm), 20 g; 2) b.p. 127-129° (0.5 mm), 5 g.

The substance with b.p. 87.5-88° (0.5 mm) is a light-green, mobile liquid with the same properties as dioxide (IV); it is the dioxide, 4,7-dimethyl-3,7-diepoxy-5-decyne (VII).

n^{20}D 1.4565, d$^{20}_{20}$ 0.9388, MR$_D$ 56.23; calc. 55.90.

Found %: C 74.40, 74.30; H 9.38, 9.47. M 192. $C_{12}H_{18}O_2$. Calculated %: C 74.23; H 9.28. M 194.

The substance with b.p. 127-129° (0.5 mm) is a light-yellow, viscous liquid, soluble in organic solvents, insoluble in water.

n^{20}D 1.4690, d$^{20}_{20}$ 1.0202, MR$_D$ 69.34; calc. 68.17.

Found %: C 66.51, 66.59; H 8.50, 8.93. M 256. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66. M 254.

The data correspond to the monoxy-alcohol-acetate, 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol (VIII).

Hydrolysis of 4,7-dimethyl-3,7-diepoxy-5-decyne (VII). 3 g of the dioxide was hydrolyzed with 1% H_2SO_4 under the same conditions as for the dioxide (IV). The aqueous layer was collected and evaporated to a small bulk on a water bath. The residue thickened on cooling. Ether was added and the mixture was stirred. Crystals came down and were collected and washed with ether 3 times. 0.4 g of erythritol was obtained: 4,7-dimethyl-5-decyn-3,4,7,8-tetralol (IX) with m.p. 157-158°.

Found %: C 62.42, 62.34; H 9.32, 9.28. $C_{12}H_{22}O_4$. Calculated %: C 62.61; H 9.56.

Oxidation of 3,6-diethyl-2,6-octadien-4-yne (III) by acetyl hydroperoxide. The hydrocarbon was prepared by dehydration of 3,6-diethyl-4-octyn-3,6-diol [5] and agreed in properties with the literature data [6]. 67 g of the hydrocarbon (b.p. 68-69° at 0.5 mm) was oxidized in a medium of anhydrous ethyl ether with 90 g of acetyl hydroperoxide (71.9%) (2 moles hydroperoxide to 1 mole hydrocarbon) at 0°. Oxidation proceeded for 15 days as established by iodometric determinations. The reaction products were isolated by the same procedure as for previous preparations. Three substances were isolated: 1) b.p. 85.5-86° (0.5 mm), 42 g; 2) b.p. 125-127° (0.5 mm), 10 g; 3) m.p. 77°, 1.9 g.

The substance with 85.5-86° (0.5 mm) is a light-yellow liquid with the same properties as the previously described dioxides.

n^{20}D 1.4596, d$^{20}_{20}$ 0.9384, MR$_D$ 56.6; calc. 55.9.

Found %: C 74.38, 74.40; H 9.26, 9.22. M 182. $C_{12}H_{18}O_2$. Calculated %: C 74.23; H 9.28. M 194.

The analytical data correspond to the dioxide, 3,6-diethyl-2,6-diepoxy-4-octyn (X).

The substance with b.p. 125-127° (0.5 mm) is a greenish-yellow, viscous liquid. It dissolves in ethyl ether, chloroform, ethyl alcohol and benzene; it is insoluble in water.

n^{20}D 1.4700, d$^{20}_{20}$ 1.0227, MR$_D$ 69.40; calc. 68.17.

Found %: C 66.33, 66.04; H 8.99, 8.94. M 251.4. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66. M 254.

The analytical data correspond to 3,6-diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol (XII).

The substance with m.p. 77° was isolated after 10-days' standing of the intermediate fraction with b.p. 121-138° (1 mm) obtained on fractional distillation of the product of oxidation of hydrocarbon (III) by acetyl hydroperoxide. It was twice recrystallized from ethyl ether.

Found %: C 67.44, 67.42; H 9.31, 9.35. M 214. $C_{12}H_{20}O_3$. Calculated %: C 67.83; H 9.43. M 212.

The analytical data identify it as the glycol-monoxide, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol (XI).

The presence of a triple bond in the monoxides and dioxides was confirmed by quantitative bromination in chloroform or benzene solution. Results of bromination are presented in Table 2 and 3.

TABLE 2

Monoxide	Weight of monoxide (in g)	Bromine needed for addition to the triple bond (in g)	
		found	calculated
(VIII) 4,7-Dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol	0.2612	0.3188	0.3290
(XI) 3,6-Diethyl-2-epoxy-4-octyn-6,7-diol	0.1840	0.2731	0.2777
(XII) 3,6-Diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol	0.2450	0.2974	0.3086

TABLE 3

Dioxide	Weight of dioxide (in g)	Bromine needed for addition to the triple bond (in g)	
		found	calculated
(IV) 6,9-Dimethyl-5,9-diepoxy-7-tetradecyne	0.3650	0.4495	0.4672
(VII) 4,7-Dimethyl-3,7-diepoxy-5-decyne	0.4815	0.7584	0.7942
(X) 3,6-Diethyl-2,6-diepoxy-4-octyne	0.1652	0.2616	0.2725

We see from the tables that bromine adds on substantially in the theoretical amount required for addition of four bromine atoms to a triple bond.

SUMMARY

1. We oxidized the divinylacetylenic hydrocarbons, 6,9-dimethyl-5,9-tetradecadien-7-yne, 4,7-dimethyl-3,7-decadien-5-yne, and 3,6-diethyl-2,6-octadien-4-yne with acetyl hydroperoxide and obtained the dioxides of these compounds: 6,9-dimethyl-5,9-diepoxy-7-tetradecyne, 4,7-dimethyl-3,7-diepoxy-5-decyne, 3,6-diethyl-2,6-diepoxy-4-octyne. We also obtained their derivatives: 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn-10-ol, 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol and 3,6-diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol.

2. The presence of a triple bond in these compounds was confirmed by quantitative bromination.

3. Hydrolysis of the dioxides, 6,9-dimethyl-5,9-diepoxy-7-tetradecyne and 4,7-dimethyl-3,7-diepoxy-5-decyne gave the erythritols, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol and 4,7-dimethyl-5-decyn-3,4,7,8-tetralol.

Received February 8, 1957

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*Original Russian pagination. See C. B. translation.

OXIDATION OF VINYLACETYLENIC HYDROCARBONS BY ORGANIC HYDROPEROXIDES

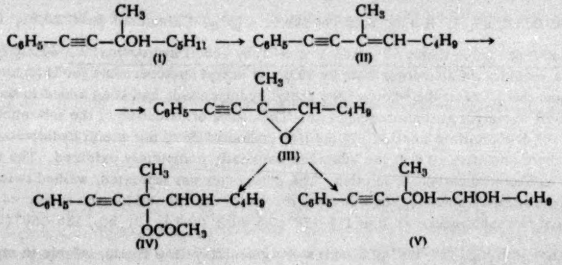
VI. OXIDATION OF 1-PHENYL-3-METHYLOCTEN-3-YNE-1 BY ACETYL HYDROPEROXIDE

N. M. Malenok and S. D. Kul'kina

The present work is a continuation of our investigations on the oxidation of vinylacetylenic hydrocarbons by acetyl hydroperoxide [1, 2].

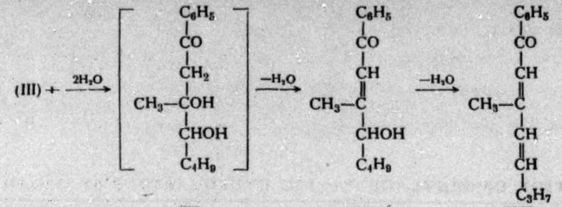
We employed the method of Zh. I. Iotsich to synthesize 1-phenyl-3-methyl-1-octyn-3-ol (I) from ethynylbenzene and methyl amyl ketone. This was dehydrated by potassium bisulfate to the hydrocarbon 1-phenyl-3-methyl-3-octen-yne-1 (II). Oxidation of hydrocarbon (II) by 80% acetyl hydroperoxide gave two substances: the acetylenic oxide, 1-phenyl-3-methyl-3-epoxy-1-octyne (III), and the acetylenic alcohol-acetate, 1-phenyl-3-methyl-3-acetoxy-1-octyn-4-ol (IV). The latter was formed by reaction of oxide (III) with acetic acid. Hydrolysis of oxide (III) by 1% H_2SO_4 gives the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol (V).

The secondary products of the reaction (alcohol-acetates, acetates, glycols) are easily formed if the oxide ring of the acetylenic hydrocarbon is linked to secondary and tertiary or tertiary carbon atoms [1].



We subjected oxide (III) to hydration by the M. G. Kucherov reaction and isolated two substances: an unsaturated ketoalcohol, 1-phenyl-3-methyl-2-octen-4-ol-1-one (VII), and a dienic ketone, 1-phenyl-3-methyl-2,4-octadien-1-one (VIII).

The following mechanism may be advanced for the formation of compounds (VII, VIII). Treatment of oxide (III) with mercuric sulfate solution leads to addition of two molecules of water; one of them adds at the site of rupture of the oxide ring and the second at the acetylenic bond. A ketoglycol – 1-phenyl-3-methyl-3,4-octanediol-1-one (VI) – is presumably first formed; we did not isolate this product. On dehydration, this substance forms the unsaturated ketoalcohol (VII) which on further loss of a molecule of water gives the dienic ketone (VIII).



(VI) (VII) (VIII)

Simultaneous hydration and dehydration by the M. G. Kucherov reaction was first observed by us in the case of 1-phenylethynylcyclohexene-1 oxide [2].

EXPERIMENTAL

Synthesis of 1-phenyl-3-methyl-1-octyn-3-ol (I). The acetylenic alcohol (I) was prepared by the Zh. I. Iotsich reaction from 102 g of ethynylbenzene (b.p. 141-143° at 750 mm) and 114 g of methyl amyl ketone (b.p. 148-151° at 750 mm) in a medium of absolute ether. The compound is a colorless, viscous liquid, soluble in organic solvents. Yield 146.5 g (70%).

B.p. 139.5-140° (0.5 mm), $n^{20}D$ 1.5257, d^{20}_{20} 0.9487, MR_D 69.85; calc. 67.39.

Found %: C 82.92, 83.03; H 9.54, 9.40. M 213.4. $C_{15}H_{20}O$. Calculated %: C 83.33; H 9.26. M 216.

Preparation of 1-phenyl-3-methyl-3-octen-1-yne (II). 75.3 g of alcohol (I) was heated at 30-40° in vacuo (26 mm) with 29 g of anhydrous potassium bisulfate. Dehydration of the alcohol commenced immediately, and the liberated water was distilled off in the course of 10 minutes. The product was extracted with ether and the extract dried with potassium carbonate. The ether was driven off and the residue subjected to two fractional distillations to give 57.3 g (83%) of a light-yellow substance.

B.p. 107-108° (0.5 mm), $n^{20}D$ 1.5465, d^{20}_{20} 0.9114, MR_D 68.95; calc. 65.40.

Found %: C 90.50, 90.57; H 9.32, 9.22. M 198.5. $C_{15}H_{18}$. Calculated %: C 90.91; H 9.09. M 198.

Oxidation of 1-phenyl-3-methyl-3-octen-1-yne (II) by acetyl hydroperoxide. 40.8 g of hydrocarbon (II) was oxidized in a medium of anhydrous ether by 20.4 g of acetyl hydroperoxide (80%) (1 mole of hydroperoxide per mole of hydrocarbon). After the whole of the acetyl hydroperoxide had been added to the substance, the reaction mass was left overnight at room temperature. The course of oxidation of the substance was checked daily by titration with 0.1 N thiosulfate solution. In the first 24 hours 70% of the acetyl hydroperoxide had reacted with the hydrocarbon, and after 10 days the substance was nearly completely oxidized. The reaction product was neutralized with 10% sodium carbonate solution. The ether layer was separated, washed twice with water and then dried with potassium carbonate. The ether was driven off and the residue was subjected to two fractional distillations to give two substances: 1) b.p. 117-118° (0.5 mm), 29.1 g; 2) b.p. 155-156° (0.5 mm), 4 g.

The substance with b.p. 117-118° (0.5 mm) was a greenish-yellow liquid, soluble in organic solvents, insoluble in water. It slowly liberates iodine from potassium iodide solution acidified with sulfuric acid, does not liberate methane when treated with methyl magnesium iodide, and slowly decolorizes a chloroform solution of bromine.

$n^{20}D$ 1.5270, d^{20}_{20} 0.9572, MR_D 68.57; calc. 66.01.

Found %: C 83.91, 83.81; H 8.43, 8.55. M 209. $C_{15}H_{18}O$. Calculated %: C 84.11; H 8.41. M 214.

The properties and analysis of this substance correspond to the acetylenic monoxide — 1-phenyl-3-methyl-3-epoxy-1-octyne (III).

The compound with b.p. 155-156° (0.5 mm) is a viscous, poorly mobile liquid, soluble in ether, ethyl alcohol and chloroform; insoluble in water. It is the alcohol-acetate — 1-phenyl-3-methyl-3-acetoxy-1-octyn-4-ol (IV).

$n^{20}D$ 1.5288, d^{20}_{20} 1.0404, MR_D 81.19; calc. 78.28.

Found %: C 75.25, 75.55; H 7.96, 7.62; OH 6.54. M 262. $C_{17}H_{22}O_3$. Calculated %: C 74.45; H 8.03; OH 6.25; M 274.

Hydrolysis of oxide (III). 2 g of the oxide was boiled with 14 ml of 1% sulfuric acid solution (frequent shaking) for 8 hours. The thickened upper layer was dissolved in ether. The ethereal layer was separated, washed with sodium carbonate solution and then with water, and dried by anhydrous sodium sulfate. The ether was distilled off and the residual mass crystallized on standing. The crystals were dissolved in ethyl alcohol and precipitated from the solution with water. The substance was twice purified in this manner and then had m.p. 81°.

Found %: C 76.28, 76.29; H 9.10, 9.02; OH 14.73. M 239. $C_{15}H_{20}O_2$. Calculated %: C 77.58; H 8.62; OH 14.65. M 232.

The compound is the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol (V).

Hydration of oxide (III) by the M. G. Kucherov reaction. 6 g of the oxide was heated with 22 ml of a solution of mercuric sulfate acidifed with sulfuric acid (3.5 g of $HgSO_4$, 2.5 ml of conc. H_2SO_4 and 75 ml of water). At 30° the solution acquired an orange-red color. Increase of temperature to 40° caused the reaction to go very vigorously and the temperature rose further. The reaction mixture was therefore cooled with water and the temperature was not allowed to rise above 40°. A grey precipitate came down after 30 minutes and the reaction was completed. The product was extracted with ether and filtered. The ethereal extract was dried with sodium sulfate. The ether was distilled off, and the residue fractionally distilled three times to give 2.3 g of product.

B.p. 124-126° (4 mm), $n^{20}D$ 1.5581, d^{20}_{20} 0.9913. MR_D 69.62; calc. 66.95.

Found %: C 83.55, 83.43; H 8.76, 8.78. M 204. $C_{15}H_{18}O$. Calculated %: C 84.11; H 8.41. M 214.

The substance rapidly decolorizes bromine in chloroform solution; with 2,4-dinitrophenylhydrazine it forms a red tarry precipitate from which pure crystals could not be isolated; it reacts very weakly with methyl magnesium iodide. It may be suggested that the substance is the dienic ketone, 1-phenyl-3-methyl-2,4-octadiene-1-one (VIII) with a very small admixture of the unsaturated ketoalcohol (VII) which lowers the carbon content and results in a value of 0.15 OH group on analysis.

The presence of two double bonds was proven by bromination of the compound in chloroform.

0.240 g of substance added 0.351 g of bromine. Calculated 0.359 g of bromine for two double bonds.

The last fraction, obtained after isolation of the dienic ketone (VIII), partly crystallized. Recrystallization from aqueous alcohol gave 0.3 g of substance with m.p. 70°.

Found %: C 76.95; H 8.08. M 232.8. $C_{15}H_{20}O_2$. Calculated %: C 77.58; H 8.62. M 232.0.

The substance is clearly the unsaturated ketoalcohol – 1-phenyl-3-methyl-2-octen-4-ol-1-one (VII).

SUMMARY

1. Oxidation of 1-phenyl-3-methyl-3-octen-1-yne by acetyl hydroperoxide gave two substances: the acetylenic oxide, 1-phenyl-3-methyl-3-epoxy-1-octyne, and the alcohol-acetate, 1-phenyl-3-methyl-3-acetoxy-1-octyn-4-ol. Hydrolysis of the oxide gave the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol.

2. Hydration of the oxide by the M. G. Kucherov reaction gave the unsaturated ketoalcohol, 1-phenyl-3-methyl-2-octen-4-ol-1-one, and the dienic ketone, 1-phenyl-3-methyl-2,4-octadien-1-one.

Received February 14, 1957

Minsk Institute of Medicine

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*Original Russian pagination. See C. B. Translation.

2-PHENYL-3-BROMOBUTENE-2 IN THE GRIGNARD REACTION

V. I. Pansevich-Koliada

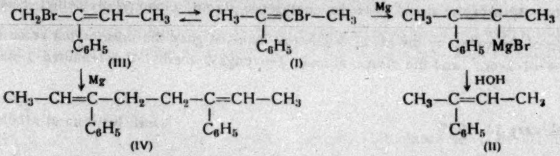
2-Phenyl-3-bromobutene-2 (I) was first prepared by bromination of 2-phenylbutene-2 (II) [1]. The same bromide is also formed on bromination of 2-phenylbutanol-2 in anhydrous solvents [2].

The action of alcoholic alkali on 2-phenyl-3-bromobutene-2 leads to the unsaturated ether 2-phenyl-4-ethoxybutene-2 [3]. The reaction goes with great facility, which indicates the great mobility of the halogen at the double bond of compound (I).

In the present work we studied the behavior of 2-phenyl-3-bromobutene-2 (I) in the Grignard reaction. Reaction starts at once when bromide (I) is added to magnesium in ether, and it goes vigorously to completion, but only one-half of the magnesium reacts. Decomposition of the reaction mixture by water proceeds with scarcely any liberation of heat, in contrast to the behavior of the usual organomagnesium compounds. The main product of the reaction was a hydrocarbon with the empirical formula $C_{20}H_{32}$ (IV), i.e., the carbon skeleton of the bromide (I) is doubled. The hydrocarbon 2-phenylbutene-2 (II) was found in the 1st fraction; it is always formed in small quantity.

The structure of hydrocarbon (IV) was confirmed by oxidation of potassium permanganate, potassium dichromate and chromic anhydride. Diphenacyl and acetic acid were found in all cases in the reaction products. The same substances were also obtained on decomposition of the ozonide of the hydrocarbon (IV). Formation of diphenacyl and acetic acid in the present case could only proceed through oxidation of 3,6-diphenyloctadiene-2,6 (IV), so that the latter, contrary to our earlier suggestion [4], is the main product of the reaction of 2-phenyl-3-bromobutene-2 (I) with magnesium.

Formation of hydrocarbon (IV) undoubtedly proceeds through a series of intermediate processes during reaction of magnesium with bromide (I). In ethereal solution a tautomeric transformation occurs between 2-phenyl-3-bromobutene-2 (I) and its isomer (formed in solution) – 2-phenyl-1-bromobutene-2 (III). Bromide (III), like other halides of the allylic type [5-8], undergoes a Wurtz reaction with magnesium to form 3,6-diphenyloctadiene-2,6 (IV). Bromide (III) reacts quickly with magnesium and this is therefore the main direction of reaction. At the same time the normal reaction of magnesium with bromide (I) takes place to a very small extent and leads to hydrocarbon (II). The processes can be represented by the equations:



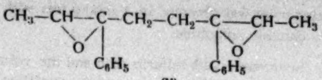
$$\underset{(III)}{CH_2Br-\underset{C_6H_5}{\underset{|}{C}}=CH-CH_3} \rightleftarrows \underset{(I)}{CH_3-\underset{C_6H_5}{\underset{|}{C}}=CBr-CH_3} \xrightarrow{Mg} CH_3-\underset{C_6H_5}{\underset{|}{C}}=\underset{MgBr}{\underset{|}{C}}-CH_3$$

$$\downarrow Mg \qquad\qquad \downarrow HOH$$

$$\underset{(IV)}{CH_3-CH=\underset{C_6H_5}{\underset{|}{C}}-CH_2-CH_2-\underset{C_6H_5}{\underset{|}{C}}=CH-CH_3} \qquad \underset{(II)}{CH_3-\underset{C_6H_5}{\underset{|}{C}}=CH-CH_3}$$

In the present case the isomeric transformation of the bromides (I and III) is similar to the well-known isomeric transformation of chlorobutenes-2 [9].

We oxidized 3,6-diphenyloctadiene-2,6 (IV) by acetyl hydroperoxide. The resultant dioxide – 3,6-diphenyl-2,3,6,7-diepoxyoctane (V) – is unstable and undergoes slight modification on distillation in vacuo.



(V)

EXPERIMENTAL

Preparation of 3,6-diphenyloctadiene-2,6 (IV). The starting bromide (I) was prepared by the action of bromine on 2-phenylbutanol-2 in chloroform [2].

B.p. 118-120° (11 mm), $n^{20}D$ 1.5811, d^{20}_4 1.3348, MR_D 52.66; calc. 52.08.

40 g of bromide (I) was added gradually (with progressive entry into reaction) to 20 g of magnesium turnings in ether. The reaction started quickly and proceeded vigorously to the end. After the whole of the bromide had been added, the mixture was heated on a water bath for an hour. When the reaction was completed, the mixture was homogeneous, andonly after standing overnight did a very small quantity of stout crystals form on the walls of the flask. The reaction mixture was decomposed by water; very slight heat development occurred on addition of the water. The ether layer was separated, the aqueous layer was extracted with ether and the extract added to the ether layer which was then dried with $MgSO_4$. After removal of the ether, the reaction products were distilled to give the following fractions: 1st, 40-139°, 6.1 g; 2nd, 130-155°, 0.8 g; 3rd, 155-158°, 16.2 g; 4th, 158-165°, 1.0 g; a small residue remained in the flask.

The 3rd fraction was redistilled to give 14.9 g of hydrocarbon (IV) in the form of a yellowish, oily and slightly opalescent liquid.

B.p. 156-157° (2 mm); $n^{20}D$ 1.5750, d^{20}_4 0.9880, MR_D 87.63; calc. 86.42.

Found %: C 91.06; H 8.57; M 247.7, 250.9. $C_{20}H_{22}$. Calculated %: C 91.22; H 8.78. M 262.

Redistillation of the 1st fraction gave a colorless, mobile liquid in a quantity of 2 g; this was 2-phenylbutene-2 (II).

B.p. 46.5 -48° (3 mm), $n^{20}D$ 1.5962, d^{20}_4 0.9156, MR_D 44.03; calc. 44.31.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by chromic anhydride. 3 g of the hydrocarbon was dissolved in 15 ml of glacial acetic acid and 4 g of chromic oxide in 30 ml of glacial acetic acid was gradually added (cooling to 5-10°). Oxidation was energetic. The reaction mixture was diluted with water and the reaction products extracted with a mixture of ether and benzene. The solvent was distilled off to leave 0.35 g of crystalline substance, poorly soluble in ether, very poorly soluble in chloroform, and more soluble in benzene. The compound does not contain active hydrogen; when dissolved in concentrated sulfuric acid it forms a green solution which becomes reddish-brown with a green fluorescence when gently heated. M.p. 145.5-146.5° (from benzene).

Found %: C 80.56; H 6.21. M 221.6. $C_{16}H_{14}O_2$. Calculated %: C 80.67; H 5.88. M 238.

The data correspond to diphenacyl [10]. The semicarbazide was prepared: m.p. 199-201° (from ethyl alcohol).

Oxidation of 3,6-diphenyloctadiene-2,6 by permanganate and dichromate in an aqueous medium goes very slowly due to its extremely poor solubility in water. The reaction products were diphenacyl, benzoic acid (m.p. 121°) and acetic acid; the silver salt of the latter was prepared.

Found %: Ag 65.02. $C_2H_3O_2Ag$. Calculated %: Ag 64.64.

Benzoic acid was undoubtedly formed by oxidation of the diphenacyl.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by ozone. 3 g of the hydrocarbon was dissolved in 20 g of chloroform and ozonized oxygen was passed through.* The chloroform was distilled off in vacuo without heating. An oily ozonide and a small amount of crystals remained in the flask. Water was added to the ozonide, and the flask contents were refluxed on a boiling water bath for 6 hours. The aqueous solution had an acid reaction. The acids were neutralized with water, and the neutral reaction products were extracted with ether-benzene mixture.

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* It should be remarked that the reaction mixture caught fire when an attempt was made to ozonize this hydrocarbon in hexane.

The solvents were distilled off to leave colorless crystals which after recrystallization from benzene melted at 146-147°. No depression of melting point was observed in a mixed test with the crystals obtained on oxidation of 3,6-diphenyloctadiene-2,6 by chromic anhydride.

The salts of the acids were decomposed with sulfuric acid and the volatile acids were distilled off with steam by boiling the solution of the acids. The first portions of the distillate gave a silver salt of a volatile acid on treatment with silver carbonate.

Found %: Ag 64.25. $C_2H_3O_2Ag$. Calculated %: Ag 64.64.

Consequently, decomposition of the ozonide had given diphenacyl and acetic acid. No other products were detected.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by acetyl hydroperoxide. To 60 g of hydrocarbon dissolved in 100 ml of absolute ether was added 100 g of 38% acetyl hydroperoxide at 20-28°. Oxidation was completed in 7 days. The acetic acid was washed out with water, and the ethereal solution was dried with sodium sulfate. Distillation (3 mm) of the oxidation products gave the following fractions: 1st, up to 193°, 15 g; 2nd, 193-197°, 29 g; 3rd, 197-204°, 9 g. Each fraction was a viscous, noncrystallizing oil with a light-yellow color and possessing an odor of active oxygen. The compound dissolved in benzene, chloroform, acetone and other organic solvents.

Found %: C 79.04; H 7.64. M 280.5, 284.5. $C_{20}H_{22}O_2$. Calculated %: C 81.59; H 7.48. M 294.

The dioxide (VI) was contaminated with some other substance containing active hydrogen. Redistillations of the dioxide resulted in progressive lowering of the percentage of carbon, due undoubtedly to slight decomposition of the dioxide at its fairly high boiling point. Derivatives of dioxide (VI) could not be prepared.

SUMMARY

1. Reaction of 2-phenyl-3-bromobutene-2 with magnesium in ether gives mainly 3,6-diphenyloctadiene-2,6.

2. Oxidation of 3,6-diphenyloctadiene-2,6 by acetyl hydroperoxide gives a dioxide – 3,6-diphenyl-2,3-6,7-diepoxyoctane – which partly decomposes on distillation due to its high boiling point.

Received February 10, 1957

Belorussian Polytechnic Institute

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* Original Russian pagination. See C. B. translation.

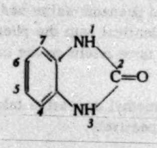
** In Russian.

INVESTIGATIONS ON IMIDAZOLE DERIVATIVES

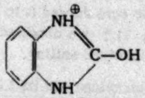
XIX. AMINO DERIVATIVES OF BENZIMIDAZOLONE AND 1,3-DIMETHYLBENZIMIDAZOLONE

L. S. Efros and A. V. El'tsov

It was shown earlier [1, 2] that in a strongly acidic medium benzimidazolone (I) and its N,N'-dimethyl derivative do not differ in reactivity and spectral absorption from derivatives of benzimidazole. This justifies the assumption that during salt formation a proton joins on at their carbonyl oxygen with formation of cations (II) and (III).



(I)



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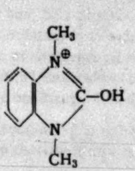

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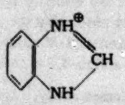

(IV)

The upsetting of the equivalence of the single and double bonds in the benzene ring of such cations is comparable with that in naphthalene [3].

In a neutral medium, however, benzimidazolone exists in the o-phenyleneurea form [2], and therefore, its heteroring differs from the imidazole ring. For this reason it appeared to us of interest to study the effect of the imidazolone ring on the benzene ring condensed with it and to attempt to establish the character of the deformation of the electron cloud in the latter.

With this objective we undertook an investigation of the chemical properties of the isomeric 4- and 5-amino derivatives of both benzimidazolone and its 1,3-dimethyl analog. The latter are not less interesting because similarity between their reactivity and that of derivatives of unmethylated benzimidazolone could serve as yet another proof of the o-phenyleneurea structure of benzimidazolone.

We prepared the amines by reduction of the corresponding nitro derivatives with tin and conc. hydrochloric acid. The free amines are easily oxidized by atmospheric oxygen, and we therefore preferred to work with their hydrochlorides.

It was found that 4-aminobenzimidazolone and its 1,3-dimethyl analog are very much less basic than the corresponding 5-amino derivatives. A similar difference in basic properties was also observed in the series of the isomeric 4- and 5-aminobenzimidazoles [4] (Table 1). These substances react differently with diazonium salts.

TABLE 1

Compound	pK_{base}*
4-Aminobenzimidazolone	10.76
5-Aminobenzimidazolone	9.00
4-Amino-1,3-dimethylbenzimidazolone	10.94
5-Amino-1,3-dimethylbenzimidazolone	9.11

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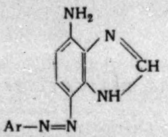
* The basicity constants were measured with a LP-4 lamp potentiometer with a pH electrode at the point of half-equivalence at 18°.

4-Aminobenzimidazole entered smoothly into the azo-coupling reaction and formed an azo dye with the azo group at the carbon atom in the 7-position (V); 5-aminobenzimidazole only formed diazoamino compounds (VI) on reaction with diazotized aromatic amines.



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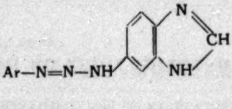
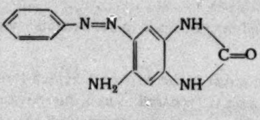


(VI)

The isomeric 4- and 5-aminobenzimidazolones that we synthesized behaved in exactly the opposite manner; 5-aminobenzimidazolone and its 1,3-dimethyl analog readily entered into the azocoupling reaction with diazotized aniline, whereas the 4-amino derivative only coupled with diazotized p-nitroaniline, and formed a diazoamino compound with the less active diazo component.

It was very important to establish the position in the molecule where 5-aminobenzimidazolone enters into the azocoupling reaction. The azo dye, obtained by coupling 5-aminobenzimidazolone with diazotized aniline, was reduced with tin in hydrochloric acid, and the mixture of reduction products was treated with an aqueous solution of the bisulfite derivative of phenanthrenequinone. After the separated phenanthrazine had been recrystallized, its absorption spectrum in concentrated sulfuric acid showed it to be identical with the phenanthrazine obtained from 5,6-diaminobenzimidazolone [5, 6] (Fig. 1).* We obtained the same results in the case of the dye from 5-amino-1,3-dimethylbenzimidazolone and diazotized aniline.

Consequently, azocoupling of 5-aminobenzimidazolone and its 1,3-dimethyl derivative takes place at the carbon atom in the 6-position with formation of azo dyes (VII) and (VIII) respectively.



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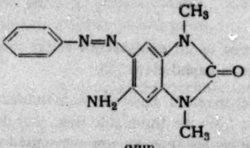

(VIII)

The identical chemical behavior of the amino derivatives both of the unsubstituted benzimidazolone and of its 1,3-dimethyl analog bears witness to the identical influence of the heterorings of these compounds on the benzene rings condensed with them and, consequently, also bears witness to the sameness of structure of the heterorings themselves, as was demonstrated earlier by other methods [2].

The observed facts enable us to assume that in 5-aminobenzimidazolone as well as in its 1,3-dimethyl derivative, the equivalence of the bonds of the benzene ring is upset, the double-bond character in the 5,6-position being sharply increased (I). The consequence is that azocoupling of the 5-amino derivatives occurs in the 6-position. If this hypothesis is correct, then a similar deformation of the electron cloud occurs in the benzene ring of the unsubstituted benzimidazolone, for otherwise it would be difficult to account for the differing reactivities of 5-aminobenzimidazole and 5-aminobenzimidazolone. It should be noted that destruction of bond equivalence of this type is of general interest since it had never previously been observed except in the case of hydrindene [7], and the conclusions drawn from this are now considered to be erroneous [8].

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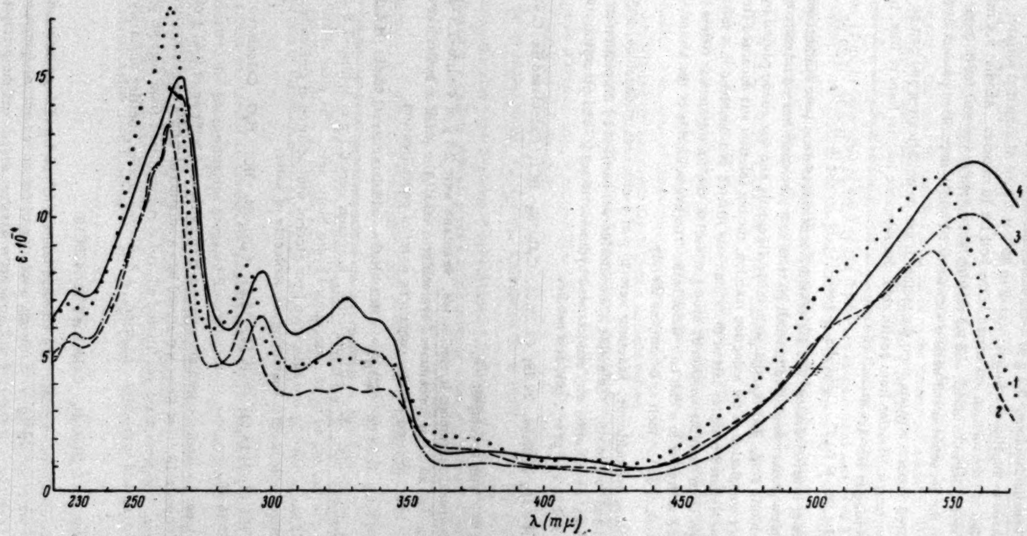
* The absorption spectra were prepared with the SF-4 spectrophotometer in screw-top quartz cells with a layer thickness of 0.5 cm and solution concentrations of 2×10^{-5} to 7×10^{-5} mole/liter. The slight differences in the extinction coefficients, in spite of the complete identity in the absorption character, can be attributed to experimental errors due to the low concentrations of the solutions.



Ultraviolet absorption spectra of phenanthrazines in concentrated sulfuric acid. 1) Phenanthrazine from 5,6-diaminobenzimidazolone; 2) phenanthrazine from products of reduction of 5-amino-6-(phenylazo)-benzimidazolone; 3) phenanthrazine from 5,6-diamino-1,3-dimethylbenzimidazolone; 4) phenanthrazine prepared from products of reduction of 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone.

EXPERIMENTAL

4-Nitro-1,3-dimethylbenzimidazolone. 3.1 g of 4-nitrobenzimidazolone was dissolved in 70 ml of 4% NaOH, and dropwise addition was made to the stirred solution (heated to 80°) of 3.4 ml of dimethyl sulfate; thereupon 10 ml of 30% NaOH was added and the solution was stirred at the boil for 10 minutes. Another 3.4 ml of dimethyl sulfate was then added and very little solid alkali, and the solution was stirred at the boil for 30 minutes. The precipitate was filtered from the hot solution and washed with water. Yield of unpurified product 30%.

Incompletely methylated products separate from the mother liquor on acidification and can be again subjected to methylation. After recrystallization from acetic acid, the substance has the form of fine, lustrous, greenish-yellow crystals, melting at 190-192.5°.

Found %: C 52.44; H 4.00; N 20.27. $C_9H_9O_3N_3$. Calculated %: C 52.17; H 4.38; N 20.28.

The amino derivatives of benzimidazolone and 1,3-dimethylbenzimidazolone were synthesized by reduction of the nitro products. The nitro product was added in small portions to a previously heated mixture of granulated tin and concentrated hydrochloric acid. The reaction went fairly vigorously and was accompanied by considerable evolution of heat. After completion of the reduction reaction, the hot solution was decanted from the tin residues and cooled. The precipitated complex salt of the amine was filtered and dissolved in a suitable quantity of water; the tin was brought down from the solution by hydrogen sulfide, the tin sulfide was filtered off and the mother liquor was evaporated to dryness in a dish on a water bath. The hydrochloride of the amine was purified. The hydrochlorides of the amines do not melt or decompose sharply.

4-Aminobenzimidazolone hydrochloride. Reactants were 36 g of 4-nitrobenzimidazolone, 175 ml of concentrated hydrochloric acid and 70 g of tin. The amine hydrochloride was purified by dissolution in hot water, treatment with animal charcoal and dilution with concentrated hydrochloric acid. The precipitate was filtered off and dried at 60-70°. Yield 23 g of heavy, colorless needles.

Found %: C 44.88; H 4.57; N 22.54, 22.79; Cl 19.25. $C_7H_7ON_3 \cdot HCl$. Calculated %: C 45.29; H 4.34; N 22.64; Cl 19.10.

The picrate melts at 241° with decomposition.

4-Amino-1,3-dimethylbenzimidazolone hydrochloride. Reactants were 2.3 g of 4-nitro-1,3-dimethylbenzimidazolone, 4 g of tin, and 20 ml of concentrated hydrochloric acid. The yield of hydrochloride was 75%. It crystallizes from water as long, colorless needles containing water of crystallization.

Found %: C 46.84; H 5.88; N 18.28. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 46.66; H 6.10; N 18.14.

5-Amino-1,3-dimethylbenzimidazolone hydrochloride. Reactants were 6.1 g of 5-nitro-1,3-dimethylbenzimidazolone [1], 10.5 g of tin, and 40 ml of concentrated hydrochloric acid. The yield of amine hydrochloride was 80%. The salt was purified by crystallization from alcohol with addition of concentrated hydrochloric acid. Colorless, microscopic needles containing one molecule of water.

Found %: C 47.05; H 5.84; N 18.01; Cl 15.56, 15.61. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 46.66; H 6.10; N 18.14; Cl 15.30.

Coupling of 4-aminobenzimidazolone with diazotized p-nitroaniline. A solution of 0.43 g of 4-aminobenzimidazolone hydrochloride in 10 ml of water was stirred into a solution of 0.55 g of p-nitrophenyldiazonium fluoborate in 30 ml of water. The precipitate was filtered off, twice recrystallized from aqueous pyridine, treated with boiling 2% acetic acid, washed with water, and dried. A dark-grey powder, melting unsharply at 298° with decomposition.

Found %: N 28.12, 28.32. $C_{13}H_{10}O_3N_6$. Calculated %: N 28.18.

5-Amino-6-(phenylazo)-benzimidazolone. To a cooled solution (0°) of 7 g of 5-aminobenzimidazolone hydrochloride in 150 ml of water was added, with stirring, a solution of diazotized aniline (prepared in the usual manner) in the theoretical quantity. An excess of sodium acetate was then added, and the precipitated azo dye was filtered after 30 minutes. Purification was effected by reprecipitation from alkali with acetic acid. The product was reduced.

A sample for analysis was obtained by crystallizing part of the product from 4% aqueous sodium carbonate solution and then from dilute hydrochloric acid. The hydrochloride of 5-amino-6-(phenylazo)-benzimidazolone is a black, amorphous powder which does not melt at 325°.

Found %: N 24.11, 24.16. $C_{13}H_{11}ON_5 \cdot HCl$. Calculated %: N 24.18.

5-Amino-6-(phenylazo)-1,3-dimethylbenzimidazolone. Excess of sodium acetate was stirred into a solution, cooled to 0°, of 7 g of 5-amino-1,3-dimethylbenzimidazolone hydrochloride in 150 ml of water; a solution of aniline diazotized in the usual manner was then added in the theoretical quantity. The precipitated azo dye was filtered after 30 minutes and subjected to reduction without purification.

The same dye was prepared for analytical purposes by running together solutions of 0.96 g of the amine hydrochloride in 40 ml of water and of 0.8 g of the fluoborate of diazotized aniline in 30 ml of water. Sodium acetate was added to the mixture and the precipitated dye was filtered off. The precipitate was recrystallized from dilute hydrochloric acid. 5-Amino-6-(phenylazo)-1,3-dimethylbenzimidazolone hydrochloride is a black, amorphous powder without a sharp melting point and decomposing at 245°.

Found %: N 22.31, 22.13. $C_{15}H_{15}ON_5 \cdot HCl$. Calculated %: N 22.04.

Reduction of the azo dyes of the 5-amino derivatives was effected with tin in concentrated hydrochloric acid. The reaction mass was diluted with water, the tin was brought down with hydrogen sulfide, the tin sulfide was filtered off, and the solution was evaporated to dryness in vacuo. The dry salt was dissolved in water and excess of the bisulfite compound of phenanthrenequinone was added to the solution. After 5 hours, the precipitated phenthrazine was filtered off and crystallized from a suitable solvent.

The phenanthrazine from 5-amino-6-(phenylazo)-benzimidazolone was crystallized from aqueous pyridine and then treated with 2% boiling aqueous acetic acid. A yellow powder, not melting at 320°. Very sparingly soluble in organic solvents; can be recrystallized from a large volume of acetic acid. Gives a bright crimson color with concentrated sulfuric acid.

Found %: N 16.94, 16.95. $C_{21}H_{12}ON_4$. Calculated %: N 16.66.

The phenanthrazine from 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone crystallized from a large volume of dioxan ; a yellow powder; gives a bright crimson color with concentrated sulfuric acid.

Found %: N 15.37, 15.59. $C_{23}H_{16}ON_4$. Calculated %: N 15.38.

5,6-Diamino-1,3-dimethylbenzimidazolone. Reaction components were 6.3 g of 5,6-dinitro-1,3-dimethylbenzimidazolone [1], 20 g of tin and 45 ml of concentrated hydrochloric acid. The hydrochloride of the diamine is very easily soluble in water and is not salted out by concentrated hydrochloric acid. The free base can be isolated by addition of sodium acetate to a concentrated aqueous solution of the hydrochloride. It forms a colorless powder, very sparingly soluble in organic solvents. Its melting point is above 320°. Small quantities of moisture promote oxidation of the diamine by atmospheric oxygen, so that it must be stored in a vacuum-desiccator over P_2O_5.

The diamine was identified through its phenanthrazine whose absorption spectrum and elemental composition corresponded to the phenanthrazine prepared from 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone.

5,6-Diaminobenzimidazolone was prepared earlier [5, 6]. We synthesized it in 70% yield by reduction of 5,6-dinitrobenzimidazolone with tin and concentrated hydrochloric acid. The diamine was converted by the method described above into the phenanthrazine, whose absorption spectrum and elemental composition identified it with the phenanthrazine from 5-amino-6-(phenylazo)-benzimidazolone.

SUMMARY

5-Aminobenzimidazolone and its 1,3-dimethyl derivative differ from 5-aminobenzimidazole by entering into the azocoupling reaction. This leads to an azo dye containing the azo group in the 6-position. This direction of the azocoupling reaction may serve as proof of the presence in the benzene ring of benzimidazolone of an intensified double-bond character between carbon atoms 5 and 6.

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Received March 11, 1957

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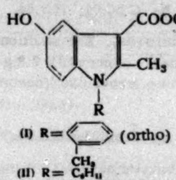
INVESTIGATIONS ON QUINONES

XXII. THE SYNTHESIS OF SUBSTITUTED INDOLES

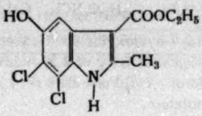
A. N. Grinev, I. A. Zaitsev, V. I. Shvedov and A. P. Terent'ev

Reaction of p-quinones with esters of β-aminocrotonic acid and its closest analogs leads, as we know, to 5-hydroxy-substituted indoles and benzindoles [1-4]. Our investigations also revealed that imines of acetylacetone react in two ways with p-benzoquinone to give either substituted indoles [3, 5] or benzofurans [4, 5].

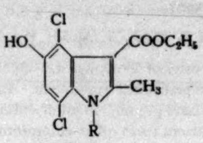
We have now succeeded in broadening the scope of this reaction somewhat. Condensation of ethyl β-aminocrotonate and some of its analogs with p-benzoquinone, 2,3-dichloro-p-benzoquinone, 2,5-dichloro-p-benzoquinone and α-naphthoquinone gave the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), the ethyl ester of 1-cyclohexyl-2-methyl-5-hydroxyindole-3-carboxylic acid (II), the ethyl ester of 2-methyl-5-hydroxy-6,7-dichloroindole-3-carboxylic acid (III), the ethyl ester of 2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (IV), the ethyl ester of 1-ethyl-2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (V) and the ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzoindole-3-carboxylic acid (VI).



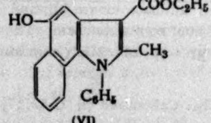
(I) R= (ortho)
(II) R= C_6H_{11}



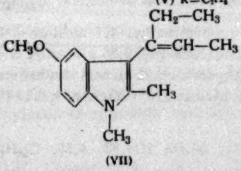
(III)



(IV) R=H
(V) R=C_2H_5



(VI)



(VII)

In addition, we studied the transformations of substituted indoles – methylated and benzoylated hydroxyindoles prepared in the present work and in preceding studies [2-6] – and the interaction of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid with ethyl magnesium bromide. The latter reaction goes smoothly when a mixture of ether and benzene is used as solvent and leads to 1,2-dimethyl-3-(2'-penten-3'-yl)-5-methoxyindole (VIII).

EXPERIMENTAL

Ethyl ester of N-(o-tolyl)-β-aminocrotonic acid. 26 g of ethyl acetoacetate was mixed with 21.5 g of o-toluidine. 2 drops of concentrated hydrochloric acid were added to the resultant solution which was then stood overnight in the cold. Ether was added to the emulsified liquid, the ether layer was dried with sodium sulfate, and the ether was distilled off to leave an oil which was distilled at reduced pressure. Yield of ester 33 g.

B.p. 136-138° (5 mm), $n^{20}D$ 1.5550, d^{20}_4 1.048, MR_D 67.17; calc. 67.24.

Found %: C 71.22, 71.43; H 7.86, 7.91. $C_{13}H_{17}O_2N$. Calculated %: C 71.20; H 7.82.

Ethyl ester of N-cyclohexyl-β-aminocrotonic acid. The reaction was carried out as in the preceding experiment, starting with 26 g of ethyl acetoacetate and 23 g of cyclohexylamine. Yield of ester 30.5 g.

B.p. 108-110° (2 mm), n^{20}_D 1.4879, d^{20}_4 1.001, MR_D 60.81; calc. 61.02.

Found %: N 6.80, 6.95. $C_{12}H_{21}O_2N$. Calculated %: N 6.63.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I). To a solution of 5.4 g of p-benzoquinone in 15 ml of anhydrous acetone was added 17 g of ethyl N-(o-tolyl)-β-aminocrotonate with stirring and cooling. The mixture was heated for 1.5 hours on the water bath, and the resulting crystals of the indole (I) were filtered and washed with a little ether. The mother liquor was concentrated on the water bath to remove the acetone, and ether was added to the viscous oil. The resulting crystals were collected. After recrystallization from alcohol the yield of ethyl 1-(p-tolyl)-2-methyl-5-hydroxyindole-3-crotonate (I) was 4.2 g; m.p. 208-209°.

Found %: C 73.65; 73.68; H 6.35, 6.23. $C_{19}H_{19}O_3N$. Calculated %: C 73.76; H 6.19.

Ethyl ester of 1-cyclohexyl-2-methyl-5-hydroxyindole-3-carboxylic acid (II). The reaction was carried out as in the preceding experiment, starting with 5.4 g of p-benzoquinone, 16 g of ethyl N-cyclohexyl-β-aminocrotonate and 15 ml of acetone. The crystals of the indole were separated by addition of ether to the reaction liquid. Yield 5 g; m.p. 69°.

Found %: C 71.80, 71.79; H 7.74, 7.79. $C_{18}H_{23}O_3N$. Calculated %: C 71.73; H 7.69.

Ethyl ester of 2-methyl-5-hydroxy-6,7-dichloroindole-3-carboxylic acid (III). Solutions of 3 g of 2,3-dichloro-p-benzoquinone [6] in 15 ml of chloroform and 3.45 g of ethyl β-aminocrotonate [7] in 6 ml of chloroform were mixed at room temperature. Heat was generated. The mixture was heated for 1 hour on a water bath. The resulting crystals of the indole (III) (0.9 g) were collected. From the filtrate, which was left to evaporate at room temperature overnight, was obtained a further 1.2 g of indole (III). Yield 2.1 g, m.p. 237-238° (from aqueous dioxan).

Found %: C 50.09, 50.20; H 3.79, 3.84. $C_{12}H_{11}O_3NCl_2$. Calculated %: C 50.01; H 3.84.

Ethyl ester of 2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (IV). The reaction was carried out as in the preceding experiment, starting with 7.2 g of 2,5-dichloro-p-benzoquinone [6], 7.8 g of ethyl β-aminocrotonate [7] and 15 ml of chloroform. Yield of indole (IV) 5.3 g; m.p. above 320° (decomp.) after two recrystallizations from ether-chloroform mixture.

Found %: C 49.99, 50.17; H 3.75, 3.68. $C_{12}H_{11}O_3NCl_2$. Calculated %: C 50.01; H 3.84.

Ethyl ester of 1-ethyl-2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (V). A mixture of 7.2 g of 2,5-dichloro-p-benzoquinone [6], 9.35 g of ethyl N-ethyl-β-aminocrotonate [8], and 2 g of anhydrous ammonium chloride in 10 ml of anhydrous ethyl alcohol was heated for 1 hour on a water bath. The precipitate was separated, washed with water and dried at 120°. Yield of indole (V) 3.8 g; m.p. 247-248° (from alcohol-chloroform mixture).

Found %: C 53.15, 53.46; H 4.83, 4.80. $C_{14}H_{15}O_3NCl_2$. Calculated %: C 53.17; H 4.78.

Ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzindole-3-carboxylic acid (VI). A solution of 3.2 g of α-naphthoquinone in 7.5 ml of anhydrous acetone was stirred (with cooling) with 6.1 g of ethyl N-phenyl-β-aminocrotonate [8], and the solution was heated for 1 hour on a water bath. The crystals of the benzindole (VI) were collected. The acetone was evaporated from the mother liquor and the residue treated with ether which brought down more crystals. Yield 1.7 g; m.p. 227° (from dioxan).

Found %: C 76.75, 76.80; H 5.68, 5.80; N 3.97, 4.02. $C_{22}H_{19}O_3N$. Calculated %: C 76.50; H 5.55; N 4.05.

Ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid. To a solution of 17.1 g of ethyl 1,2-dimethyl-5-hydroxyindole-3-carboxylate [2] in 200 ml of dioxan was added 18.4 g of dimethyl sulfate, followed by 172 ml of 2 N sodium hydroxide. The mixture was shaken at room temperature for 6 hours. Dilution of the dioxan solution with water brought down the ethyl ester of 1,2-dimethyl-5-methoxyindole carboxylic acid. Yield 17.2 g, m.p. 114-115° (from methanol).

Found %: C 67.95, 68.05; H 7.04, 7.05. $C_{14}H_{17}O_3N$. Calculated %: C 67.99; H 6.93.

1,2-Dimethyl-5-methoxyindole-3-carboxylic acid. A solution of 2.9 g of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid and 5.3 g of potassium hydroxide in 100 ml of ethyl alcohol were boiled for 5 hours; the alcohol was driven off and the dry residue dissolved in water. Acidification of the aqueous solution with hydrochloric acid (to Congo) gave 1,2-dimethyl-5-methoxyindole-3-carboxylic acid. Yield 1.95 g, m.p. 190-191° (from methanol).

Found %: C 65.82, 65.83; H 6.02, 6.09. $C_{12}H_{13}O_3N$. Calculated %: C 65.73; H 5.93.

1,2-Dimethyl-3-(penten-2'-yl-3')-5-methoxyindole (VII). A solution of 5 g of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid in 150 ml of anhydrous benzene was gradually added to the organomagnesium compound prepared from 1.5 g of magnesium turnings and 5 g of ethyl bromide in 150 ml of absolute ether. The reaction mixture was heated for 4 hours at boiling point. After decomposition of the organomagnesium compound in the usual manner and removal of the solvent, the 1,2-dimethyl-3-(penten-2'-yl-3')-5-methoxyindole (VII) was distilled at reduced pressure. Yield 3 g, b.p. 163-165° (6 mm), m.p. 52-53° (from methanol).

Found %: C 78.94, 79.11; H 8.63, 8.56. $C_{16}H_{21}ON$. Calculated %: C 78.97; H 8.70.

Compound (VII) differs from the starting compound in easily decolorizing an ethereal solution of bromine.

1-Phenyl-2-methyl-3-acetyl-5-methoxyindole. The reaction was performed under the conditions of preparation of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid, using 30 g of 1-phenyl-2-methyl-3-acetyl-5-hydroxyindole [3], 27.4 g of dimethyl sulfate, 240 ml of 2 N sodium hydroxide and 25 ml of dioxan. Yield of 1-phenyl-2-methyl-3-acetyl-5-methoxyindole 27.4 g ,m.p. 124-125° (from methanol).

Found %: C 77.35, 77.44; H 6.09, 5.99. $C_{18}H_{17}O_2N$. Calculated %: C 77.39; H 6.13.

Acidification of the aqueous alkaline solution led to separation of 3.1 g of unchanged starting compound.

Ethyl ester of 2-methyl-5-methoxy-6,7-dichloroindole-3-carboxylic acid. The reaction was performed under the conditions of the preceding experiment, starting with 0.6 g of ethyl ester of 2-methyl-5-hydroxy-6,7-dichloroindole-3-carboxylic acid (III), 0.5 ml of dimethyl sulfate, 10 ml of 2 N sodium hydroxide and 3 ml of dioxan. Yield of ethyl ester of 2-methyl-5-methoxy-6,7-dichloroindole-3-carboxylic acid 0.58 g, m.p. 133° (from aqueous dioxan).

Found %: C 51.62, 51.48; H 4.32, 4.39. $C_{13}H_{13}O_3NCl_2$. Calculated %: C 51.67; H 4.33.

Ethyl ester of 2-methyl-5-benzoxyindole-3-carboxylic acid.* 2.2 g of the ethyl ester of 2-methyl-5-hydroxyindole-3-carboxylic acid [2] was dissolved in 6 ml of pyridine. To the cooled solution was added 1.1 ml of benzoyl chloride and the reaction mixture was stood for 4 hours at room temperature. 100 ml of water was then added and the precipitate was collected and washed on the filter with 10% sulfuric acid (until the odor of pyridine had disappeared). The ethyl ester of 2-methyl-5-benzoxyindole-3-carboxylic acid was dried and recrystallized from alcohol. Yield 2.8 g, m.p. 175°.

Found %: C 70.33, 70.45; H 5.45, 5.47. $C_{19}H_{17}O_4N$. Calculated %: C 70.57; H 5.30.

Ethyl ester of 1-phenyl-2-methyl-5-benzoxyindole-3-carboxylic acid. The experiment was performed with 3 g of ethyl ester of 1-phenyl-2-methyl-5-hydroxyindole-3-carboxylic acid, 1.2 ml of benzoyl chloride and 9 ml of pyridine. Yield of ethyl ester of 1-phenyl-2-methyl-5-benzoxyindole-3-carboxylic acid 3.84 g, m.p. 120-121° (from dioxan).

Found %: C 75.15, 75.37; H 5.55, 5.62. $C_{25}H_{21}O_4N$. Calculated %: C 75.17; H 5.30.

Ethyl ester of 1-phenyl-2-methyl-5-benzoxybenzindole-3-carboxylic acid. The experiment was performed with 1.1 g of the ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzindole-3-carboxylic acid (VI), 0.4 ml of benzoyl chloride and 3 ml of pyridine. Yield of ethyl ester of 1-phenyl-2-methyl-5-benzoxybenzidole-3-carboxylic acid 1.3 g, m.p. 185° (from alcohol-dioxane mixture).

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* The benzoylation of other hydroxyindoles was effected by the procedure described in this experiment.

Found %: C 77.55, 77.42; H 5.36, 5.32. $C_{29}H_{23}O_4N$. Calculated %: C 77.48; H 5.16.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-benzoxyindole-3-carboxylic acid. Reaction components were 3.2 g of the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), 1.2 ml of benzoyl chloride and 6 ml of pyridine. Yield of benzoyl derivative 2.44 g; m.p. 146-147° (from alcohol).

Found %: N 3.40, 3.44. $C_{26}H_{23}O_4N$. Calculated %: N 3.39.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-(3,5-dinitrobenzoxy)-indole-3-carboxylic acid. Reaction components were 3.2 g of the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), 2.3 g of dinitrobenzoyl chloride and 9 ml of pyridine. Yield of benzoyl derivative 2.5 g, m.p. 121° (from alcohol-dioxan mixture).

Found %: C 62.18, 62.13; H 4.36, 4.32. $C_{26}H_{21}O_8N_3$. Calculated %: C 62.02; H 4.20.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-(o-methoxybenzoxy)-indole-3-carboxylic acid. The experiment was performed with 2.9 g of ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid, 1.6 g of o-methoxybenzoyl chloride and 6 ml of pyridine. Yield of benzoyl derivative 2.8 g, m.p. 171° (from alcohol).

Found %: C 72.33, 72.47; H 5.63, 5.73. $C_{28}H_{25}O_5N$. Calculated %: C 72.37; H 5.84.

Ethyl ester of 1-propionitrile-2-methyl-5-benzoxyindole-3-carboxylic acid. The experiment was carried out with 1.1 g of ethyl ester of 1-propionitrile-2-methyl-5-hydroxyindole-3-carboxylic acid [4], 0.7 g of benzoyl chloride and 8 ml of pyridine. Yield of ethyl ester of 1-propionitrile-2-methyl-5-benzoxyindole-3-carboxylic acid 1.2 g, m.p. 165° (from alcohol).

Found %: C 70.24, 70.27; H 5.30, 5.47. $C_{22}H_{20}O_4N_2$. Calculated %: C 70.20; H 5.36.

Ethyl ester of 1-ethyl-2-methyl-5-benzoxyindole-3-carboxylic acid. Reactants were 2.5 g of the ethyl ester of 1-ethyl-2-methyl-5-hydroxyindole-3-carboxylic acid [4], 1.4 g of benzoyl chloride and 12 ml of pyridine. Yield of benzoyl derivative 3.2 g, m.p. 137°.

Found %: C 72.01, 71.87; H 6.24, 6.07. $C_{21}H_{21}O_4N$. Calculated %: C 71.78; H 6.02.

SUMMARY

1. Condensation of p-quinones with the ethyl ester of β-aminocrotonic acid and its analogs gave a series of substituted hydroxyindoles.

2. A procedure for methylation and benzoylation of hydroxyindoles was developed.

3. The reaction of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid with ethyl magnesium bromide was studied.

Received December 28, 1956

Moscow State University

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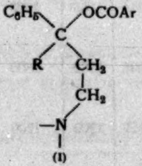
SYNTHETIC ANALGESICS

XXIV. ESTERS OF 1-PHENYL-2,2-DIMETHYL-3-DIALKYLAMINOPROPAN-1-OLS

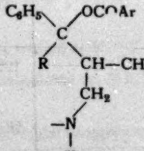
I. N. Nazarov, E. M. Cherkasova and Chan Chon Khvan

We have been engaged for some years in the search for new analgesics and anesthetics, and in preceding communications [1, 2] we described a series of esters of 1-phenyl-3-dialkylaminopropan-1-ols (I) and (II).

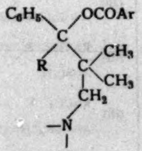
In the present paper we describe the synthesis of esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1-ols (III). They were prepared with the objective of clarifying the effect of further branching of the dialkylaminopropane chain on the physiological activity of this type of complex ester.



(I)



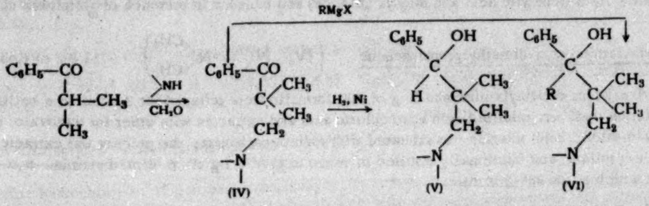
(II)



(III)

$R=H,\ CH_3,\ C_2H_5,\ C_3H_7,\ C_4H_9,\ C_5H_{11}$
$Ar=C_6H_5,\ C_6H_4OCH_3,\ C_6H_5CH=CH$ etc.

Esters (III) were synthesized by a series of routes, previously developed by us, starting from isobutyrophenone. By the Mannich reaction the latter was converted to the aminoketones (IV) which were then hydrogenated to the corresponding secondary aminoalcohols (V). By the Grignard reaction, compounds (IV) were converted into the tertiary aminoalcohols (VI).



Secondary amines employed in the Mannich reaction were dimethylamine and piperidine. Treatment of the aminoalcohols (V) and (VI) with acid chlorides gave the corresponding esters (III), which were subjected to pharmacological examination in the form of the hydrochlorides, primarily with reference to their activity as surface anesthetics. The tests established that all* of the preparations possess high anesthetic activity. The most interesting compound was found to be 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (No. 1 in table) whose activity was equal to that of dicaine but whose toxicity was very much lower. This preparation satisfactorily withstands sterilization in 0.5% solution. This ester surpasses dicaine in its ability to bring about conductive (radial) anesthesia. Investigation of the irritant action showed that this preparation in 1 and 2% solution resembles dicaine in not causing changes in the hypodermic tissue. Similar characteristics were exhibited by a number of other preparations (No. 2 to 5 in table). Consequently, the introduction of two methyl groups in the α,α-position to the carbon atom linked to hydroxyl favorably influences the pharmacological properties of the prepared esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1-ols (III), especially in respect to stability during sterilization.

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* With exception of one preparation (1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol p-nitrobenzoate) which was not tested due to its insolubility in water.

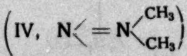
Results of the pharmacological tests (surface anesthesia) are shown in the Table.

Anesthetic Activity of Some Hydrochlorides of Esters (III) in Comparison with Dicaine

Preparation No.	Formula of preparation	Anesthetizing "index"			Anesthetizing index after sterilization (0.5%)	Mean lethal dose in mg/kg
		0.1%	0.25%	0.5%		
	Dicaine	683	1100	1300	1300	8.5
1	(III) $R{=}C_2H_5$, $N\langle\ {=}N(CH_3)_2$ $Ar{=}C_6H_4OCH_3$	618	1294	1300	1300	19
2	(III) $R{=}CH_3$, $N\langle\ {=}N(CH_3)_2$ $Ar{=}C_6H_4OCH_2CH_3$	44	314	1300	1300	24
3	(III) $R{=}CH_3$, $N\langle\ {=}N(CH_3)_2$ $Ar{=}C_6H_5$	195	908	1300	1300	31
4	(III) $R{=}CH_3$, $N\langle\ {=}N(CH_3)_2$ $Ar{=}C_6H_5CH{=}CH$	587	951	1300	1300	13.5
5	(III) $R{=}CH_3$, $N\langle\ {=}N(CH_3)_2$ $Ar{=}C_6H_4OCH_3$	337	997	1300	1276	23.5

EXPERIMENTAL

The starting isobutyrophenone was synthesized by the Friedel-Crafts reaction in 81% yield from isobutyryl chloride (prepared from isobutyric acid and thionyl chloride) and benzene in presence of aluminum chloride [3].



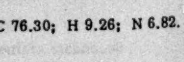
$\left(IV,\ N\langle = N\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\right)$

β-Dimethylamino-α,α-dimethylpropiophenone $\left(IV,\ N\langle = N\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\right)$. 14.8 g of isobutyrophenone [3], 72 g of 25% aqueous dimethylamine and 35 g of 30% formalin were refluxed for 3 hours on a boiling water bath. The reaction mass was acidified with hydrochloric acid and extracted with ether for removalof neutral products. The hydrochloric acid solution was saturated with sodium carbonate; the product was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo to give 3.1 g of β-dimethylamino-α,α-dimethylpropiophenone with b.p. 95-98° (3 mm).

Found %: C 76.78, 76.13; H 9.15, 8.97; N 6.92, 7.14. $C_{13}H_{19}ON$. Calculated %: C 76.30; H 9.26; N 6.82.

The hydrochloride of the aminoketone melted at 138-140° [7].

Found %: N 6.03. $C_{13}H_{19}ON \cdot HCl$. Calculated %: N 5.83.



$\left(IV,\ N\langle = N\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\right)$

1-Phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (V). 2.5 g of the aminoketone $\left(IV,\ N\langle = N\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\right)$

in 50 ml of anhydrous alcohol was hydrogenated in presence of 3 g of Ni catalyst for 2 hours. The volume of hydrogen absorbed was 275 ml compared with the theoretical requirement of 250 ml. The catalyst was filtered off, the alcohol was driven off, and the residue was distilled in vacuo to give 1.68 g (81%) of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 109-110° (3 mm) [4].

Found %: C 75.2, 75.57; H 10.41, 10.21; N 7.20, 6.88. $C_{13}H_{21}ON$. Calculated %: C 75.20; H 10.12; N 6.76.

The hydrochloride of the aminoalcohol melted at 174-175° (from acetone and alcohol).

Found %: N 5.42, 5.42. $C_{13}H_{21}ON \cdot HCl$. Calculated %: N 5.77.

1,2,2-Trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left[VI,\ R{=}CH_3,\ N\langle = N(CH_3)_2\right]$. An ethereal solution of methyl magnesium iodide was prepared from 3.64 g of magnesium, 29 g of methyl iodide and 57 ml of anhydrous ether. 15.5 g of β-dimethylamino-α,α-dimethylpropiophenone $\left(IV,\ N\langle = N\langle^{CH_3}_{CH_3}\right)$. was gradually stirred into the solution at 0-5°. The mixture was stirred for 2 hours at room temperature and left overnight. The next day it was stirred on a water bath at the boiling point of ether for about 2 hours. After cooling, the reaction mass was treated with saturated ammonium chloride solution, the neutral products were twice extracted with ether, and the acid layer was saturated with sodium carbonate. The resulting oil was repeatedly extracted with ether and dried with sodium sulfate. Yield 11.95 g (71.5%) of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with b.p. 103-104° (2 mm).

Found %: C 76.23, 76.31; H 9.74, 10.47; N 6.22, 6.21. $C_{14}H_{23}ON$. Calculated %: C 76.20; H 10.2; N 6.32.

The hydrochloride of the aminoalcohol melted at 85-86° (from acetone).

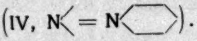
Found %: N 5.34. $C_{14}H_{23}ON \cdot HCl$. Calculated %: N 5.42.

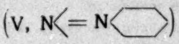
1-Ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(VI,\ R{=}C_2H_5,\ N\langle = N\langle^{CH_3}_{CH_3}\right)$. To a solution of ethyl magnesium bromide, prepared from 1.41 g of magnesium, 6.5 g of ethyl bromide and 22 ml of anhydrous ether, was gradually added dropwise with stirring at 0-5° 6.04 g of the aminoketone $[IV,\ N\langle = N(CH_3)_2]$. The product was worked up as described above. Yield 5.2 g (75%) of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 118-119° (3mm).

Found %: C 76.31, 76.89; H 10.75, 11.01; N 5.55, 5.79. $C_{15}H_{25}ON$. Calculated %: C 76.6; H 10.62; N 5.92.

The hydrochloride of the aminoalcohol melted at 224-225°.

Found %: C 66.34, 66.75; H 9.51, 9.27; N 5.31. $C_{15}H_{25}ON \cdot HCl$. Calculted %: C 66.31; H 9.58; N 5.18.

α,α-Dimethyl-β-piperidylpropiophenone . 44.4 g of isobutyrophenone, 36.4 g of piperidine hydrochloride, 12 g of paraformaldehyde, 300 ml of dioxan and 0.5 ml of hydrochloric acid were heated on a boiling water bath until the paraformaldehyde had completely dissolved. The material was worked up in the usual manner to give 20.3 g (27.6%) of α,α-dimethyl-β-piperidylpropiophenone with b.p. 122-125° (2 mm); the hydrochloride had m.p. 157-158° (from acetone) (this aminoketone was obtained in a yield of 4% [5]).

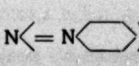
1-Phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol [6] . 9.8 g of α,α-dimethyl-β-piperidylpropiophenone in 100 ml of alcohol was hydrogenated in presence of nickel catalyst (prepared from

11 g of 75% alloy) with continuous shaking for 8 hours. 1060 ml of hydrogen was absorbed instead of 966 ml required by theory. The catalyst was filtered off, the alcohol was driven off, and the residue was acidified. The neutral products were extracted with ether and the aqueous acidic layer was treated with caustic alkali and repeatedly extracted with ether. After drying of the ether extract and removal of the ether, 9.8 g (99%) of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol was obtained with m.p. 74-75°.

Found %: N 6.03, 6.16. $C_{16}H_{25}ON$. Calculated %: N 5.70.

The hydrochloride melted at 223-224° (from acetone and alcohol).

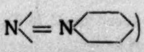
Found %: N 5.37, 5.52. $C_{16}H_{25}ON \cdot HCl$. Calculated %: N 4.95.

1,2,2-Trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (VI, R = CH_3, ). 11.14 g of α,α-dimethyl-β-piperidylpropiophenone in 20 ml of ether was gradually stirred at −10° into an ethereal solution of methyl magnesium iodide prepared from 3.8 g of magnesium, 20.2 g of methyl iodide and 60 ml of anhydrous ether. The next day the reaction mass was acidified, the neutral products were separated by extraction with ether, and the aqueous acid layer was treated with 20% alkali solution and repeatedly extracted with ether. After drying and removal of the ether, the product was fractionally distilled in vacuo to give 6.25 g (53%) of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with b.p. 120-124° (2 mm).

Found %: N 5.31, 5.19. $C_{17}H_{27}ON$. Calculated %: N 5.35.

The hydrochloride melts at 195-196° (from acetone and alcohol).

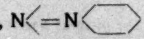
Found %: N 4.72, 4.88. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.73.

1-Ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (VI, R = C_2H_5, ). 24.5 g of α,α-dimethyl-β-piperidylpropiophenone was added under the above conditions to an ethereal solution of ethyl magnesium bromide prepared from 7.2 g of magnesium, 36.3 g of ethyl bromide and 50 ml of ether. The material was worked up as in the preceding experiment to give 23.4 g (85%) of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 57-58°.

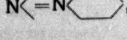
Found %: N 5.06, 5.31. $C_{18}H_{29}ON$. Calculated %: N 5.09.

The hydrochloride melted at 221-222° (from alcohol-acetone mixture).

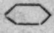
Found %: N 4.47, 4.64. $C_{18}H_{29}ON \cdot HCl$. Calculated %: N 4.48.

Phenoxyacetate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (III, R = H, , Ar = $CH_2OC_6H_5$). 5 g of phenoxyacetyl chloride in 30 ml of chloroform was added at −10° to a solution of 4.94 g of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol in 30 ml of chloroform in presence of 0.1 g of magnesium. The following day the chloroform was distilled off. The residue was twice washed with ether, the ether was poured off and a fresh portion of ether was added. The precipitate was boiled for 30 minutes and recrystallized from a mixture of chloroform and acetone. Yield 4.94 g (59.2%) of the hydrochloride of the phenoxyacetate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 193-194°.

Found %: C 69.33, 69.42; H 7.18, 7.37; N 3.55, 3.65. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69; H 7.69; N 3.36.

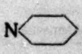
Phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (III, R = CH_3, , Ar = $CH_2OC_6H_5$). Reactants were 5.22 g of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, 0.1 g of magnesium, 5 g of phenoxyacetyl chloride in 30 ml of chloroform. The mixture was heated for 2 hours on a water bath at 50-60°. The following day the solvent was driven off in a low vacuum and the oily residue dissolved in 50 ml of anhydrous acetone and a little ether. 7.56 g of technical product with m.p. 80-84° was isolated. It was recrystallized from chloroform to give 5.12 g (59.5%) of the hydrochloride of the phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with m.p. 94-95°.

Found %: N 3.50, 3.57. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: N 3.24.

Phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (III, R = C_2H_5, N = N 

Ar = $CH_2OC_6H_5$). mixture of 5.51 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol, 3.6 g of phenoxyacetyl chloride, 0.1 g of magnesium and 60 ml of chloroform was heated for 2 hours on a water bath, after which dry hydrogen chloride was passed through the solution. The solvent was driven off in a low vacuum, and the residue was dissolved in a 1 : 1 mixture of chloroform and acetone. Cooling brought down the hydrochloride of the original aminoalcohol which did not show a depression of melting point in admixture with an authentic specimen. Ether was added to the mother liquor until the thick oil had completely separated; the latter was dried in a vacuum-desiccator for 40-50 hours using a powerful water jet pump. A cotton wool-like precipitate of the hydrochloride of the phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol was formed; yield 1.95 g (21.9%); m.p. 135-138° (from acetone).

Found %: C 69.90, 70.10; H 8.03, 8.19; N 3.32, 3.33, $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 69.9; H 8.1; N 3.14.

Benzoate of 2,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (III, R = H, $N\langle$ = $N\langle$ ,

Ar = C_6H_5). A mixture of 4.95 g of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)propan-1-ol, 4.22 g of benzoyl chloride, 0.1 g of magnesium and 50 ml of chloroform was kept at room temperature for 24 hours and then heated for 1 hour at 50-60°. The magnesium granules were separated, the solvent was distilled off, and the residue was recrystallized from a 3 : 1 acetone-chloroform mixture. Yield 6.29 g (81.3%) of the hydrochloride of the benzoate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 193-195°.

Found %: C 71.71, 71.57; H 7.98, 7.69; N 3.68, 3.51. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: C 71.40; H 7.75; N 3.62.

Cinnamic ester of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, R = H, $N\langle = N\langle^{CH_3}_{CH_3}$,

Ar = $C_6H_5CH=CH$). A mixture of 2.07 g of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol, 5 ml of anhydrous benzene, 3.3 g of cinnamyl chloride and 0.1 g of magnesium was heated for 1.5 hours on a boiling water bath. The next day the solvent was distilled off in vacuo, and the residue was dissolved in water and acidified with hydrochloric acid. The neutral products were extracted with ether several times. The aqueous layer was treated with sodium carbonate, the liberated base was extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo to give 1.2 g (35.5%) of the cinnamic ester of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 180° (2 mm), m.p. 85-86°.

Found %: C 78.92, 79.55; H 7.74, 7.82; N 4.40, 4.47. $C_{22}H_{27}O_2N$. Calculated %: C 78.50; H 7.98; N 4.17.

The hydrochloride melted at 129-130° (from acetone).

Found %: N 3.39, 3.32. $C_{22}H_{27}O_2N \cdot HCl$. Calculated %: N 3.74.

Phenoxyacetate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, R=H, $N\langle = N\langle^{CH_3}_{CH_3}$,

Ar = $CH_2OC_6H_5$). 3.41 g of phenoxyacetyl chloride in 5 ml of benzene was gradually run with cooling into a solution of 2.07 g of 1-phenyl-2,2-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. Heating and crystallization of the whole mass were observed. Anhydrous ether was added and the mixture heated for 2 hours at the boiling point of ether. The latter was run off; the solid was washed several times with ether and twice recrystallized from chloroform to give 2 g (54%) of the hydrochloride of the phenoxyacetate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 210-211°.

Found %: C 67.02, 66.50; H 7.14, 7.48; N 3.71, 3.76. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: C 66.80; H 7.41; N 3.71.

Benzoate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = H, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = C_6H_5\right)$. Under the conditions of the preceding experiment, 2.07 g of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 2.81 g of benzoyl chloride were reacted to give 2.2 g (63%) of the hydrochloride of the benzoate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 201-202° (from acetone and alcohol).

Found %: C 68.97, 69.23; H 7.48, 7.23; N 3.87, 4.13. $C_{20}H_{25}O_2N \cdot HCl$. Calculated %: C 69.10; H 7.49; N 4.04.

Phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = CH_3, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = CH_2OC_6H_5\right)$. 2.35 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 5.45 g of phenoxyacetyl chloride in 10 ml of anhydrous benzene were kept for 12 hours at 0°. The material was then worked up as in the preceding experiment to give 2.2 g (59%) of the hydrochloride of the phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 117-118° (from acetone).

Found %: C 67.84, 67.73; H 7.36, 7.84; N 3.34, 3.42. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 68.10; H 7.72; N 3.61.

Cinnamic ester of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = CH_3, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = C_6H_5CH{=}CH\right)$. Under conditions similar to those described above, 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.33 g of cinnamyl chloride in 5 ml of anhydrous benzene gave 2.5 g (62%) of the hydrochloride of the cinnamate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 204-205°.

Found %: C 71.20, 71.32; H 7.78, 7.49; N 3.96, 3.92. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: C 71.20; H 7.74; N 3.62.

Benzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = CH_3, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = C_6H_5\right)$. Reactants were 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-ol and 3 g of benzoyl chloride in 5 ml of anhydrous benzene. The reaction mass was worked up as in the preceding experiments to give 2.5 g (69%) of the hydrochloride of the benzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 202-205° (from chloroform and anhydrous alcohol).

Found %: C 69.48, 69.54; H 8.06, 8.03; N 4.10, 3.89. $C_{21}H_{27}O_2N \cdot HCl$. Calculated %: C 69.80; H 7.75; N 3.88.

p-Nitrobenzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = CH_3, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = C_6H_4NO_2\text{-}p\right)$. 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.71 g of p-nitrobenzoyl chloride in 15 ml of anhydrous benzene, reacted under the above-described conditions, gave 3.35 g (84%) of the hydrochloride of the p-nitrobenzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 205-206° (from acetone and anhydrous alcohol).

Found %: C 62.53, 62.33; H 6.41; 6.89; N 6.99, 6.88. $C_{21}H_{26}O_4N_2 \cdot HCl$. Calculated %: C 62.00; H 6.14; N 6.90.

Phenoxypropionate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol $\left(\text{III}, R = CH_3, N\!< \; = N\!<^{CH_3}_{CH_3}, Ar = CH_2CH_2OC_6H_5\right)$. 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.71 g of phenoxypropionyl chloride in 5 ml of anhydrous benzene were heated for 2 hours on a boiling water bath. Anhydrous ether was then added and the whole mass was triturated. The ether was run off, a fresh portion of ether was added, and the trituration was repeated until the oil-like slurry started to solidify, after which 5 ml of anhydrous acetone was added and the resultant precipitate was recrystallized from chloroform to give 0.5 g (12.5%) of the hydrochloride of the phenoxypropionate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 174-175°

Found %: C 67.73, 67.84; H 7.67, 7.82; N 3.64, 3.77. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.00; H 7.88; N 3.46.

Cinnamic ester of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(\mathrm{III},\ R=C_2H_5,\ N\!\!<\ = N\!\!<^{CH_3}_{CH_3},\ Ar=C_6H_5CH{=}CH\right)$. 3.33 g of cinnamyl chloride was added to 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. After 2-hours' heating on a boiling water bath, crystals began to come down. These were worked up with anhydrous ether to give 1.7 g (42.5%) of the hydrochloride of the cinnamate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 186-186.5° (from anhydrous alcohol).

Found %: C 71.57, 71.65; H 7.75, 8.09; N 3.12, 3.40. $C_{24}H_{31}O_2N\cdot HCl$. Calculated %: C 71.80; H 7.98. N 3.48.

Phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(\mathrm{III},\ R=C_2H_5,\ N\!\!<\ = N\!\!<^{CH_3}_{CH_3},\ Ar=CH_2OC_6H_5\right)$. 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 3.41 g of phenoxyacetyl chloride in 5 ml of anhydrous benzene were reacted under the conditions of the preceding experiment to give 2.2 g (54.5%) of the hydrochloride of the phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 148-149° (from acetone).

Found %: C 67.96; H 7.63; N 3.35, 3.70. $C_{23}H_{31}O_3N\cdot HCl$. Calculated %: C 68.00; H 7.88; N 3.45.

Benzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(\mathrm{III},\ R=C_2H_5,\ N\!\!<\ = N\!\!<^{CH_3}_{CH_3},\ Ar=C_6H_5\right)$. Under the above-described conditions, 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 2.81 g of benzoyl chloride in 8 ml of anhydrous benzene gave 1.8 g (48%) of the hydrochloride of the benzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 168-169° (from anhydrous alcohol).

Found %: N 4.36, 4.21. $C_{22}H_{29}O_2N\cdot HCl$. Calculated %: N 3.74.

p-Nitrobenzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol $\left(\mathrm{III},\ R=C_2H_5,\ N\!\!<\ = N\!\!<^{CH_3}_{CH_3},\ Ar=C_6H_4NO_2\text{-}p\right)$ Reaction as above between 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 3.71 g of p-nitrobenzoyl chloride in 8 ml of anhydrous benzene gave 2.2 g (52.5%) of the hydrochloride of the p-nitrobenzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 176-177° (from chloroform).

Found %: C 62.67, 62. 46; H 6.75, 6.60; N 6.85, 6.75. $C_{22}H_{28}O_4N_2\cdot HCl$. Calculated %: C 62.80; H 6.70; N 6.69.

SUMMARY

1. A series of esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1-ols with a branched propanol chain was synthesized for the purpose of pharmacological tests. Aminoketones and aminoalcohols with dimethylamine and piperidine residues were also obtained as intermediate products.

2. Some of the synthesized compounds exhibited high anesthetic activity. The phenoxyacetate of 1-ethyl-2,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol is equivalent to dicaine in anesthetizing activity but is considerably less toxic and is stable when sterilized in 0.5% solution.

Received December 14, 1956

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Fine Chemical Technology

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[3] Sabatier and Mailhe, Compt. rend., 158, 833 (1914); Braun and Senattner, Ber., 74, 22 (1941).

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ACETYLENE DERIVATIVES

190. PREPARATION OF ETHOXYACETYLENE AND ITS EMPLOYMENT FOR THE SYNTHESIS OF UNSATURATED ALDEHYDES AND ACIDS

I. N. Nazarov, Zh. A. Krasnaia and V. P. Vinogradov

At the start of our investigations on the synthesis of polyenic compounds and isoprenoids, we considered the possibility of using ethoxyacetylene for this purpose.

Alkoxyacetylenes were first prepared by A. E. Favorskii and M. N. Shchukina [1] in 25% yield from vinyl ethers. Another method was developed by Jacobs [2] whereby β-bromovinylalkyl ethers are obtained from acetals of bromoacetaldehyde in 18% yield. Eglinton and coworkers described a new method of preparation of alkoxyacetylenes from haloacetals in one step by the action of sodium amide in liquid ammonia; yield 60% [3]. This method suffers, however, from a number of disadvantages associated with working with liquid ammonia, the very large consumption of sodium and the danger of explosion due to the exceptional sensitivity of the sodium derivative of ethoxyacetylene to the air.

The use of ethoxyacetylene has been limited in the past by its difficult accessibility due to the complexity of the methods of preparation.

We prepared ethoxyacetylene by a modification of the method of A. E. Favorskii and M. N. Shchukina, starting from vinyl ethyl ether. The latter was brominated in the absence of a solvent by adding it to cooled bromine [4]. This procedure excludes secondary reactions and leads to exhaustive bromination of vinyl ethyl ether. The so-prepared α,β-dibromodiethyl ether was used for preparation of β-bromovinyl ethyl ether without prior distillation. Considerable difficulties had attended the preparation of β-bromovinyl ethyl ether – the principal intermediate for production of ethoxyacetylene. A repetition of the literature method [1] of preparation of β-bromovinyl ethyl ether from α,β-dibromoethyl ether showed this method to be totally unsuitable for work with large quantities (300-400 g) since the heating of α,β-dibromoethyl ether with diethylaniline in a medium of anhydrous vaseline oil at 90-95° was accompanied by sudden rise of temperature to 160° with formation of resin and a small quantity of the acetal of bromoacetaldehyde.

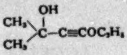
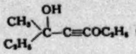
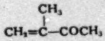
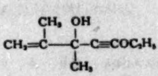
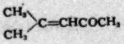
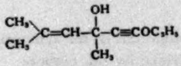
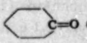
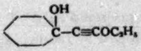
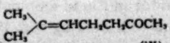
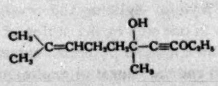
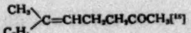
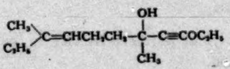
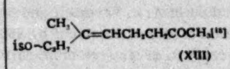
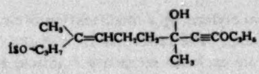
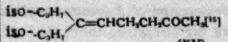
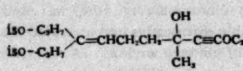
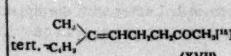
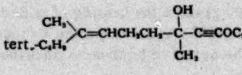
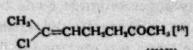
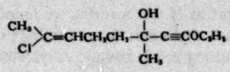
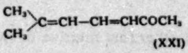
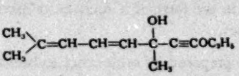
In a detailed investigation of this reaction we found that hydrogen bromide could be most conveniently split off from α,β-dibromodiethyl ether by gradual addition of the latter to diethylaniline in vacuo with simultaneous distillation of the resulting β-bromovinyl ethyl ether. The latter was obtained in 70-75% yield (on the original vinyl ethyl ether) in the form of a mixture of isomers, rectification of which in a column gave 17% of trans- and 83% of cis-isomer.

Ethoxyacetylene was prepared by subjecting β-bromovinyl ether (the mixture of isomers) to heating and mechanical stirring with pulverized potassium hydroxide in a vacuum of about 200 mm. The yield of pure ethoxyacetylene was 63% (on the β-bromovinyl ether taken). An increased yield in this step was difficult to obtain because the trans-isomer of β-bromovinyl ether was recovered unchanged.

Our new method thus enables the preparation of larger quantities of ethoxyacetylene in 44% yield (on the starting vinyl ethyl ether) whereas the literature method can only be operated with small quantities and the yield is only 25%.

It is well-known that ethoxyethynyl magnesium bromide readily enters into reaction with ketones to form

TABLE 1

No.	Starting ketones	Ethoxyethynyl carbinols	Yield (in %)
1	CH_3COCH_3	 $(CH_3)_2C(OH)-C\equiv COC_2H_5$ (I)	77*
2	$CH_3COC_2H_5$	 $(CH_3)(C_2H_5)C(OH)-C\equiv COC_2H_5$ (II)	68.5*
3	 $CH_2=C(CH_3)-COCH_3$ (III)	 $CH_2=C(CH_3)-C(OH)(CH_3)-C\equiv COC_2H_5$ (IV)	55*
4	 $(CH_3)_2C=CHCOCH_3$ (V)	 $(CH_3)_2C=CH-C(OH)(CH_3)-C\equiv COC_2H_5$ (VI)	63*
5	 (VII)	 (VIII)	76*
6	 $(CH_3)_2C=CHCH_2CH_2COCH_3$ (IX)	 $(CH_3)_2C=CHCH_2CH_2C(OH)(CH_3)-C\equiv COC_2H_5$ (X)	92
7	 $(CH_3)(C_2H_5)C=CHCH_2CH_2COCH_3$[16] (XI)	 $(CH_3)(C_2H_5)C=CHCH_2CH_2-C(OH)(CH_3)-C\equiv COC_2H_5$ (XII)	80
8	 $(CH_3)(iso\text{-}C_3H_7)C=CHCH_2CH_2COCH_3$[16] (XIII)	 $(CH_3)(iso\text{-}C_3H_7)C=CHCH_2CH_2-C(OH)(CH_3)-C\equiv COC_2H_5$ (XIV)	80
9	 $(iso\text{-}C_3H_7)_2C=CHCH_2CH_2COCH_3$[15] (XV)	 $(iso\text{-}C_3H_7)_2C=CHCH_2CH_2-C(OH)(CH_3)-C\equiv COC_2H_5$ (XVI)	70
10	 $(CH_3)(tert.\text{-}C_4H_9)C=CHCH_2CH_2COCH_3$[16] (XVII)	 $(CH_3)(tert.\text{-}C_4H_9)C=CHCH_2CH_2-C(OH)(CH_3)-C\equiv COC_2H_5$ (XVIII)	70
11	 $(CH_3)(Cl)C=CHCH_2CH_2COCH_3$[17] (XIX)	 $(CH_3)(Cl)C=CHCH_2CH_2-C(OH)(CH_3)-C\equiv COC_2H_5$ (XX)	61
12	 $(CH_3)_2C=CH-CH=CHCOCH_3$ (XXI)	 $(CH_3)_2C=CH-CH=CH-C(OH)(CH_3)-C\equiv COC_2H_5$ (XXII)	63

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* Yield based on the ethoxyacetylene taken into reaction; in the remaining cases the yield is calculated on the ketone.

ethoxyethynyl carbinols [5-7]. Addition of one molecule of hydrogen to ethoxyethynyl carbinols in presence of Pd catalyst gives ethoxyvinyl carbinols, which under the action of dilute acids are transformed into α,β-unsaturated aldehydes. Ethoxyethynyl carbinols in an acid medium are transformed into esters of α,β-unsaturated acids.

We studied the condensation of ethoxyacetylene with saturated, unsaturated and cyclic ketones. Ethoxyethynyl carbinols were synthesized by two routes: reaction of ketones with ethoxyethynyl magnesium bromide (the Iotsich reaction) and reaction of ketones with ethoxyacetylene in presence of potassium hydroxide (the Favorskii reaction).

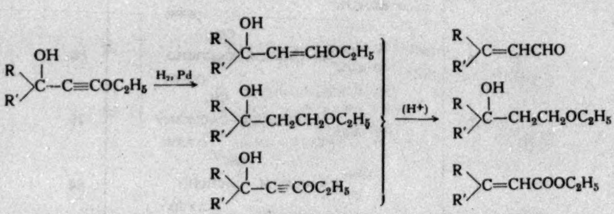
The ethoxyethynyl carbinols prepared by the first method are listed in Table 1 [all of the carbinols except (I) and (X) were synthesized for the first time]. The yield of ethoxyethynyl carbinols from saturated, cyclic and γ,δ-unsaturated ketones was 70-92%. This reaction goes the most smoothly with methylheptenone (XI) and its analogs (XI), (XIII), (XV) and (XVII). The yield of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) (starting material for the synthesis of citral) was 92% as compared with the 73% reported in the literature [7].

Addition of ethoxyethynyl magnesium bromide to α,β-unsaturated ketones [methylisopropenyl ketone (III), mesityl oxide (V) and methylheptadienone (XXXI)] takes place normally in the 1,2-position with formation of the corresponding ethoxyethynyl carbinols (yield 55-63%).

Ethoxyethynyl carbinols had previously never been obtained by the Favorskii reaction. It was found that this method gives ethoxyethynyl carbinols in lower yields than when using ethoxyethynyl magnesium bromide. Thus, the yield of dimethylethoxyethynyl carbinol (I) by the Favorskii method was 39% (against 77%), and that of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) was 58% (against 92%).

Ethoxyethynyl carbinols were hydrogenated in ethereal solution in presence of Pd catalyst to give ethoxyvinyl carbinols. In presence of 3% sulfuric or 5% oxalic acid, the latter (without distillation) are easily converted into α,β-unsaturated aldehydes (Table 2).

Hydrogenation of ethoxyethynyl carbinols in presence of Pd catalyst is not entirely selective. This is reflected in all cases in the separation of a secondary product boiling 10-15° higher than the corresponding aldehyde and having a lower refractive index. The experiment on preparation of citral, for example, gave a fraction with b.p. 75-79° (1.5 mm), $n^{21}D$ 1.4639, not possessing aldehydic properties. This fraction was exhaustively hydrogenated in presence of Pt catalyst; 1.5 moles of hydrogen per mole of compound were absorbed. The product of hydrogenation was a mixture of substances boiling at 65-73° (1.5 mm) whose empirical analysis corresponded to the formula $C_{12}H_{26}O_2$. The product of exhaustive hydrogenation is presumably a mixture of the ethyl ester of tetrahydrogeranic acid and 3,7-dimethyl-1-ethoxyoctan-3-ol. The secondary product with b.p. 75-79° (1.5 mm) formed during the preparation of citral is probably a mixture of fully hydrogenated ethoxyacetylenic carbinol and the ethyl ester of geranic acid. These secondary products are formed because the hydrogenation of the triple bond is not strictly selective.



The selectivity of hydrogenation of ethoxyacetylenic carbinols depends on their structure. Carbinols prepared from methylheptenone and its analogs are hydrogenated more selectively than carbinols synthesized from acetone, methyl ethyl ketone, cyclohexanone and other similar ketones; citral and its analogs are therefore obtained from ethoxyacetylenic carbinols in high yield (80-90%).

Hydrogenation of ethoxyacetylenic carbinols in presence of copper-nickel catalyst [13] is entirely unselective.

We observed that dialkylethoxyvinyl carbinols are converted to a considerable extent into α,β-unsaturated

aldehydes even in the absence of acid. For example, distillation of the product of partial hydrogenation of dimethylethoxyethynyl carbinol (I) gave dimethylacrolein (XXIII) in 59 % yield. This is accounted for by the facility of allylic rearrangement of ethoxyvinyl carbinols to form half acetals which are transformed into α,β-unsaturated aldehydes.

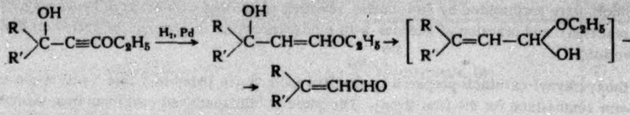
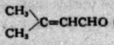
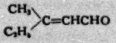
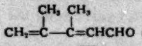
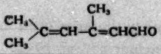
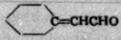
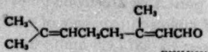
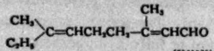
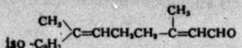
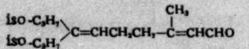
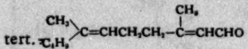
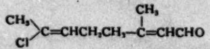
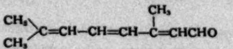


TABLE 2

Prep. No.	Aldehydes	Yield of aldehydes (in %)
1	 (XXIII)	74
2	 (XXIV)	66
3	 (XXV)	60
4	 (XXVI)	40
5	 (XXVII)	52
6	 (XXVIII)	83
7	 (XXIX)	91.6
8	 (XXX)	81
9	 (XXXI)	86
10	 (XXXII)	75
11	 (XXXIII)	84
12	 (XXXIV)	40*

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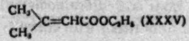
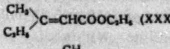
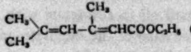
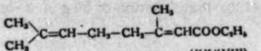
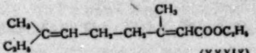
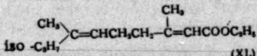
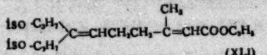
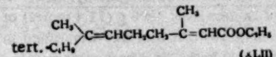
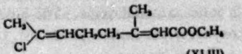
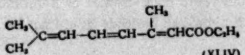
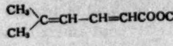
*Yield based on the methylheptadienone; in the remaining cases on the ethoxyacetylenic carbinol.

Ethoxyacetylenic carbinols are converted into ethyl esters of α,β-unsaturated acids (Table 3) in high yield under the action of 10% sulfuric acid at room temperature. Some of the prepared esters were hydrolyzed by a methanol solution of potassium hydroxide to form the corresponding α,β-unsaturated acids. In none of the numerous experiments on conversion of ethoxyacetylenic carbinols into α, β-unsaturated aldehydes and esters did we obtain β-hydroxy compounds [6].

TABLE 3

Prep. No.	Esters of acids	Yield of esters (in %)
1	 $(CH_3)_2C{=}CHCOOC_2H_5$ (XXXV)	65.5 *
2	 $(CH_3)(C_2H_5)C{=}CHCOOC_2H_5$ (XXXVI)	87
3	 $(CH_3)_2C{=}CH{-}C(CH_3){=}CHCOOC_2H_5$ (XXXVII)	62.5
4	 $(CH_3)_2C{=}CH{-}CH_2{-}CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XXXVIII)	90
5	 $(CH_3)(C_2H_5)C{=}CH{-}CH_2{-}CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XXXIX)	89
6	 $(CH_3)(\text{iso-}C_3H_7)C{=}CHCH_2CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XL)	90
7	 $(\text{iso-}C_3H_7)_2C{=}CHCH_2CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XLI)	80
8	 $(CH_3)(\text{tert.-}C_4H_9)C{=}CHCH_2CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XLII)	85
9	 $(CH_3)(Cl)C{=}CHCH_2CH_2{-}C(CH_3){=}CHCOOC_2H_5$ (XLIII)	82.5
10	 $(CH_3)_2C{=}CH{-}CH{=}CH{-}C(CH_3){=}CHCOOC_2H_5$ (XLIV)	34 *
11	$C_6H_5CH{=}CHCOOC_2H_5$ (XLV)	50 *
12	$C_3H_7CH{=}CHCOOC_2H_5$ (XLVI)	51 *
13	 $(CH_3)_2C{=}CH{-}CH{=}CHCOOC_2H_5$ (XLVII)	28.3*

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* The ethoxyacetylenic carbinol was not isolated in the pure form and the yield is therefore based on the ketone or aldehyde; in the remaining cases the yield is based on the ethyoxyethynyl carbinol.

The literature is lacking in any information about the manner of reaction of ethoxyethynyl magnesium bromide with aldehydes.** We studied the reaction of ethoxyethynyl magnesium bromide with acetaldehyde, n-butyraldehyde, dimethylacrolein and benzaldehyde. It was found that the secondary ethoxyethynyl carbinols prepared from the aldehydes are extremely unstable. Attempts to distill these substances in vacuo in a nitrogen stream led in some cases (acetaldehyde, dimethylacrolein) even at room temperature to spontaneous decomposition accompanied by intense heat liberation and formation of resin. The formation of ethoxyethynyl carbinols from aldehydes and ethoxyacetylene is nevertheless confirmed by the fact that shaking of the ethereal extracts of these carbinols, obtained after reaction, with 10% sulfuric acid resulted in separation in yields of up to 50% of the corresponding ethyl esters of α,β-unsaturated acids [Table 3, compounds (XLV)-(XLVII)].

** After the present paper had been completed and had gone to press, a paper was published on the reaction of aldehydes with ethoxyethynyl magnesium bromide [14].

EXPERIMENTAL

1. Bromination of vinyl ethyl ether. 450 g (6.25 moles) of dry, distilled vinyl ethyl ether was gradually added, with stirring and cooling to −5°, to 1000 g (6.25 moles) of bromine (pure for analysis). 1450 g of α,β-dibromodiethyl ether was obtained and was used without distillation for preparation of β-bromovinyl ethyl ether.

2. Cleavage of hydrogen bromide from α,β-dibromodiethyl ether. 2300 g of dry diethylaniline (15.4 moles) was placed in a 4-liter, 3-necked flask fitted with stirrer (vacuum seal), dropping funnel and Vigreux column (the latter connected to a sloping condenser). A vacuum of 13-15 mm was created in the system, and the diethylaniline was heated to 90-95°. Addition of 1450 g (6.25 moles) of α,β-dibromodiethyl ether was made in the course of 4 hours to the heated diethylaniline. Within a few minutes after the start of addition of the dibromo ether, β-bromovinyl ethyl ether began to distil off in admixture with a little diethylaniline. The distillate was collected in an ice-cooled receiver. Fractionation of the distillate gave 655 g (70%) of β-bromovinyl ethyl ether with b.p. 42-46° (12 mm), $n^{20}D$ 1.4700. Fractionation of 50 g of β-bromovinyl ethyl ether in an 18-plate column gave the following fractions:

a) 7.0 g (17%) of trans-isomer.

B.p. 39-40° (28 mm), $n^{20}D$ 1.4648, d^{20}_4 1.4120, MR 29.54; calc. 29.61; μ 2.36 D.*

Found %: C 31.99, 32.11; H 4.70, 4.66. C_4H_7OBr. Calculated %: C 31.81; H 4.67.

b) 34.8 g (83%) of cis-isomer.

B.p. 51-51.8° (28 mm), $n^{20}D$ 1.4750. d^{20}_4 1.4310, MR 29.63; calc. 29.61; μ 2.8.

Found %: C 31.79, 31.74; H 4.50, 4.63. C_4H_7OBr. Calculated %: C 31.81; H 4.67.

Cleavage of hydrogen bromide from β-bromovinyl ethyl ether. Ethoxyacetylene. 600 g (4 moles) of β-bromovinyl ethyl ether (mixture of isomers) and 1200 g (21.4 moles) of powdered potassium hydroxide were put into a three-necked flask. A vacuum of 180-200 mm was established in the system and the reaction mass was mechanically stirred and heated on an oil bath. At a bath temperature of 95-105° the ethoxyacetylene rapidly distilled into a receiver cooled with solid carbon dioxide. The product was dried with potassium carbonate and distilled to give 175 g (63%) of ethoxyacetylene with b.p. 22-25° (180 mm), $n^{20}D$ 1.3800 [1].

In this experiment 115 g of unreacted trans-isomer of β-bromovinyl ethyl ether was obtained (b.p. 45-47° at 28 mm, $n^{20}D$ 1.4625), from which hydrogen bromide could not be split off on treatment for a second time with potassium hydroxide.

Dimethylethoxyethynyl carbinol (I). To the ethyl magnesium bromide prepared from 9.7 g of magnesium and 47 g (0.43 mole) of ethyl bromide in 140 ml of absolute ether was gradually added (while stirring) 29.4 g (0.42 mole) of freshly distilled ethoxyacetylene in 60 ml of absolute ether. When the addition was completed, the reaction mass was heated for 15 minutes at 35° until ethane ceased to come off, after which 26 g (0.45 mole) of acetone in 25 ml of absolute ether was gradually added while being cooled with a freezing mixture. The mixture was stirred for 30 minutes at room temperature and for 15 minutes at 35°; it was then cooled with ice and treated with 20% ammonium chloride solution. The ethereal layer was separated and the aqueous layer was extracted with three portions of ether. The combined ethereal extracts were dried with calcined potassium carbonate. Distillation gave 40.2 g (77%) of dimethylethoxyethynyl carbinol (I) with b.p. 67-68° (9 mm), $n^{20}D$ 1.4428, in agreement with the literature data [6].

b) 16.8 g (0.3 mole) of pulverized potassium hydroxide and 80 ml of absolute ether were placed in a three-necked flask fitted with mechanical stirrer, dropping funnel and condenser. In the course of 45 minutes, with iced-water cooling and vigorous stirring, a mixture of 10.5 g (0.15 mole) of ethoxyacetylene and 8.7 g (0.15 mole) of acetone in 25 ml of absolute ether was added. The reaction mass was stirred for 45 minutes at 0° and for 3 hours at room temperature. Addition was then made, with iced-water cooling, of 35 ml of water; the ethereal layer was separated and the aqueous layer was extracted with ether. The ethereal extract was saturated with carbon dioxide and dried with potassium carbonate. Distillation in vacuo gave 7 g of dimethylethoxyethynyl carbinol (I) with b.p. 65-66° (11 mm).

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* Dipole moments were determined in benzene solution at 25° by the beat method in the department of physical chemistry of our institute.

β,β-Dimethylacrolein (XXIII). a) 15 g of freshly distilled dimethylethoxyethynyl carbinol (I) in 30 ml of absolute ether was hydrogenated in presence of 5% palladium deposited on calcium carbonate with cold-water cooling. After 1.5 hours 1 mole of hydrogen (2,842 ml, 758 mm, 22°) had been absorbed, and hydrogenation was stopped. After separation of the catalyst, the bright-red solution was evaporated and distilled to give the following fractions: 1st, 132-135° (760 mm), n^{19}D 1.4523, 5.8 g; 2nd, 55-59° (13 mm), n^{19}D 1.4261, 2.3 g.

The first fraction was β,β-dimethylacrolein (XXIII), the 2,4-dinitrophenylhydrazone of which melted at 179-180° [9] (from ethyl alcohol-ethyl acetate mixture); λ^{*}_{max} (in isooctane) 350, 366, 380 mμ.

b) 15.45 g of freshly distilled dimethylethoxyethynyl carbinol (I) in 30 ml of absolute ether was hydrogenated in presence of Pd catalyst (cooling with water). The calculated quantity of hydrogen (2,890 ml; 763 mm, 20°) was absorbed after 1.5 hours, and hydrogenation was stopped. After the catalyst had been separated, 5 ml of 3% sulfuric acid was added to the ethereal solution, and the mixture was shaken for 45 minutes. The ethereal layer was washed with 10 ml of 5% sodium bicarbonate solution and 10 ml of water, and dried with calcined magnesium sulfate.

Distillation gave 7.5 g of β,β-dimethylacrolein (XXIII) with b.p. 133-135° (760 mm), n^{19}D 1.4520, and 1 g of higher boiling fraction with b.p. 48-54° (10 mm), n^{19}D 1.4255.

Methylethylethoxyethynyl carbinol (II). To the ethyl magnesium bromide prepared from 6.7 g of magnesium and 30.5 g (0.28 mole) of ethyl bromide in 100 ml of absolute ether was gradually added, with stirring, 20 g (0.286 mole) of freshly distilled ethoxyacetylene. The reaction mass was heated for 15 minutes at 35° until ethane ceased to be evolved, after which 22.2 g (0.308 mole) of methyl ethyl ketone and 25 ml of ether were added to the cooled mixture. The latter was stirred for 30 minutes at room temperature, and for 45 minutes at 35°; it was then cooled with ice and treated with 20% ammonium chloride solution. The ethereal layer was separated and the aqueous layer was extracted several times with ether. The combined ethereal extracts were dried with calcined magnesium sulfate and distilled to give 27.8 g of methylethylethoxyethynyl carbinol (II).

B.p. 73-74° (8 mm), n^{20}D 1.4470, d^{20}_{4} 0.9357, MR 40.55; calc. 40.25.

Found %: C 67.29, 67.22; H 9.88, 10.10. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.88.

Ethyl ester of β-methyl-β-ethylacrylic acid (XXXVI). 10 g of methylethylethoxyethynyl carbinol (II) was shaken for 5 minutes with 100 ml of 10% sulfuric acid. The temperature of the reaction mass rose to 43°. The organic layer was collected and the aqueous layer extracted several times with ether. The ethereal solution was washed with water until neutral and dried; the ether was driven off and the residue distilled in vacuo to give 8.7 g of the ethyl ester of β-methyl-β-ethylacrylic acid (XXXVI) with b.p. 75-77° (26 mm), n^{17}D 1.4430, d^{20}_{4} 0.9114, in agreement with the literature [8].

β-Methyl-β-ethylacrolein (XXIV). 13.4 g of freshly distilled methylethylethoxyethynyl carbinol (II) in 25 ml of absolute ether was hydrogenated in a jacketed hydrogenation flask, cooled with tap water, in presence of Pd catalyst. Hydrogenation was stopped after 1 hour 20 minutes when 1 mole of hydrogen (2,400 ml; 21°, 745 mm) had been taken up. The catalyst was separated and washed with ether; 20 ml of 5% oxalic acid solution was added and the mixture stirred for an hour. The ethereal layer was separated and the aqueous layer was extracted 3 times with ether. The combined ethereal extracts were washed with 5% sodium bicarbonate solution and dried with calcined magnesium sulfate. Distillation gave 6 g of (XXIV) with b.p. 50-53° (12 mm), n^{20}D 1.4550, d^{20}_{4} 0.9040, and 3.4 g of a higher boiling fraction with b.p. 56-70° (12 mm), n^{20}D 1.4297.

The 2,4-dinitrophenylhydrazone of aldehyde (XXIV) has m.p. 169-170° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 352, 365, 380 mμ.

Found %: N 20.05, 20.25. $C_{12}H_{14}O_4N_4$. Calculated %: N 20.10.

Methylisopropenylethoxyethynyl carbinol (IV). 19.8 g (0.236 mole) of freshly distilled methylisopropenyl ketone (III) in 50 ml of absolute ether was stirred while cooling (ice and salt) into the ethoxyethynyl magnesium bromide prepared from 5.2 g of magnesium, 23.4 g (0.214 mole) of ethyl bromide and 15 g (0.214 mole) of ethoxyacetylene in 100 ml of absolute ether. The addition was made in the course of an hour and the reaction mass was then stirred for 30 minutes at 20° and for 15 minutes at 35° before being worked up as above. Yield 18 g of methylisopropenylethoxyethynyl carbinol (IV).

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*The ultraviolet spectra were measured in the optical laboratory of the Moscow State University.

B.p. 66-67° (3 mm), $n^{20}D$ 1.4640, d^{20}_4 0.9468, MR 44.82; calc. 44.39.

Found %: C 69.97, 70.59; H 9.37, 9.45; OH 10.6. $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10; OH 11.04.

2,3-Dimethylpenta-1,3-dien-5-al (XXV). 12 g of methylisopropenylethoxyethynyl carbinol (IV) in 20 ml of absolute ether was hydrogenated in presence of Pd catalyst. Hydrogenation was stopped after 4 hours when the calculated quantity of hydrogen (1980 ml; 19°, 735 mm) had been absorbed. The catalyst was separated, 10 ml of 3% sulfuric acid was added to the solution, and the mixture was thoroughly stirred for 1 hour. The following fractions were obtained after the usual working-up: 1st, b.p. 55-65° (8 mm), $n^{18}D$ 1.4790, 5.1 g; 2nd, b.p. 65-73° (8 mm), $n^{18}D$ 1.4702, 1.5 g.

Redistillation of the 1st fraction gave 4.5 g of 2,3-dimethylpenta-1,3-dien-5-al (XXV).

B.p. 59-63° (8 mm), $n^{20}D$ 1.4800, d^{20}_4 0.9151, MR 34.15; calc. 33.61.

The 2,4-dinitrophenylhydrazone of aldehyde (XXV) had m.p. 160-161° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 358, 372, 388 mμ.

Found %: N 19.43, 19.66. $C_{13}H_{14}O_4N_4$. Calculated %: N 19.31.

1-Ethoxyethynylcyclohexan-1-ol (VIII). Dropwise addition of 15.5 g (0.158 mole) of cyclohexanone in 30 ml of absolute ether was made with cooling (ice and salt) to the ethoxy ethynyl magnesium bromide prepared in the usual manner from 3.47 g of magnesium, 15.6 g (0.143 mole) of ethyl bromide and 10 g (0.143 mole) of ethoxyacetylene in 80 ml of absolute ether. The reaction mass was then stirred for 1 hour at room temperature and for 1 hour at 35° before being worked up by the usual procedure. Yield 18.2 g of 1-ethoxyethynylcyclohexan-1-ol (VIII).

B.p. 75-76° (0.02 mm), $n^{20}D$ 1.4830, d^{20}_4 1.0085, MR 47.51; calc. 47.35.

Found %: C 71.42; 71.21; H 9.13, 9.84. $C_{10}H_{16}O_2$. Calculated %: C 71.50; H 9.55.

Cyclohexylideneacetaldehyde (XXVII). 20 g of 1-ethoxyethynylcyclohexan-1-ol (VIII) was hydrogenated in solution in 30 ml of absolute ether in presence of Pd catalyst. Hydrogenation was stopped after 1.5 hours, after absorption of the calculated quantity (3,015 ml; 22°, 751 mm) of hydrogen. The catalyst was separated and 20 ml of 5% oxalic acid was added to the solution. The mixture was vigorously stirred for 1 hour and worked up as usual to give the following fractions: 1st, b.p. 50-52° (2 mm), $n^{20}D$ 1.4880; 7.7 g; 2nd, b.p. 52-60° (2 mm), $n^{20}D$ 1.4670, 3.2 g; residue 5 g.

The 1st fraction was cyclohexylideneacetaldehyde (XXVII) whose 2,4-dinitrophenylhydrazone melted at 194-195° (from ethyl alcohol-ethyl acetate mixture), in agreement with the literature [10]; λ_{max} (in isooctane) 354, 365 mμ.

Found %: N 19.64, 19.70. $C_{14}H_{16}O_4N_4$. Calculated %: N 19.66.

The semicarbazone of aldehyde (XXVII), obtained as a colorless powder, had m.p. 198-199° (from ethyl alcohol); λ_{max} (in isooctane) 273 mμ.

Found %: N 23.10, 22.91. $C_9H_{15}ON_3$. Calculated %: N 23.26.

2,6-Dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X). a) 12.6 g (0.1 mole) of freshly distilled methylheptenone (IX) (b.p. 48-49° at 6 mm) was added in the course of an hour in a nitrogen atmosphere with cooling (ice and salt) to the ethoxyethynyl magnesium bromide prepared from 3.12 g of magnesium, 16 g (0.13 mole) of ethyl bromide and 9.2 g (0.131 mole) of ethoxyacetylene in 75 ml of absolute ether. The reaction mixture was stirred for 1 hour at room temperature and for 30 minutes at 35°. It was then worked up in the usual manner to give 18 g (92%) of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X).

B.p. 79-80° (0.01 mm), $n^{20}D$ 1.4678, d^{20}_4 0.9237, MR 58.98; calc. 58.31.

Found %: C 73.27; 73.41; H 10.17, 10.15. $C_{12}H_{20}O_2$. Calculated %: C 73.41; H 10.20.

b) Into a three-necked flask, fitted with mechanical stirrer, dropping funnel and condenser topped by a calcium chloride tube, were charged 11.2 g of pulverized potassium hydroxide and 60 ml of absolute ether. A mixture of 12.6 g (0.1 mole) of methylheptenone and 8.75 g (0.125 mole) of ethoxyacetylene in 15 ml of absolute ether was added with stirring and iced-water cooling in a nitrogen stream over a period of 1 hour. The mixture was stirred with iced water cooling for 3.5 hours. 15 g of ice was then added, the ether layer was separated and the aqueous layer was extracted 3 times with ether. The ethereal extract was saturated with carbon dioxide. The product was dried with potassium carbonate and distilled to give 3 g of unreacted methylheptenone (b.p. 65-68° at 17 mm, $n^{19}D$ 1.4409) and 11.4 g (58%) of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) with b.p. 78-80° (0.01 mm), $n^{19}D$ 1.4690.

The yield is lower if the reaction period is lengthened and if the reaction is performed at a higher (room) temperature due to resinification.

Citral (XXVIII). 72.8 g of the above-described 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) was hydrogenated in 100 ml of absolute ether in presence of Pd catalyst while cooling with water. In the course of 3 hours the calculated quantity of hydrogen (9,290 ml; 21°, 753 mm) was taken up and hydrogenation was stopped. The catalyst was separated and 75 ml of 3% sulfuric acid was added to the ethereal solution which had a strong odor of lemon peel. The mixture was shaken for an hour. After working up in the usual manner, the product was distilled in vacuo to give the following fractions: 1st, b.p. 69-71° (1.5 mm), $n^{20}D$ 1.4788, 46 g; 2nd, b.p. 65-79° (1.5 mm), $n^{21}D$ 1.4639, 7.4 g; resinous residue 5.1 g. The 1st fraction was citral; λ_{max} (in heptane) 335 mμ (log ε 1.54), 347 mμ (log ε 1.55).

Found %: C 79.02, 78.74; H 10.62, 10.78. $C_{10}H_{16}O$. Calculated %: C 78.90; H 10.52.

Fractional crystallization of the prepared citral from ethyl alcohol led to isolation of the two isomeric 2,4-dinitrophenylhydrazones in a ratio of 8 : 1, orange crystals with m.p. 131-133° and bright-red crystals with m.p. 95-97°.

Crystals with m.p. 131-133°: λ_{max} (in heptane) 253, 364 mμ.

Found %: N 16.64, 16.93. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.88.

Crystals with m.p. 95-97°: λ_{max} (in heptane) 256, 365 mμ.

Found %: N 17.03, 16.87. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.88.

The constants of the 2,4-dinitrophenylhydrazones correspond to those in the literature [11].

The 2nd fraction gives neither a 2,4-dinitrophenylhydrazone nor a semicarbazone; 3 g of this fraction was subjected to exhaustive hydrogenation in 10 ml of absolute ethyl alcohol in presence of Pt catalyst. After 6 hours, 565 ml of hydrogen (20°, 744 mm) had been absorbed, corresponding to 1.5 moles of hydrogen per mole of substance. Distillation gave a liquid with b.p. 65-73° (1.5 mm), $n^{20}D$ 1.4325, consisting mainly of 2,6-dimethyl-8-ethoxyoctan-6-ol.

Found %: C 71.53, 71.49; H 12.58, 13.03. $C_{12}H_{26}O_2$. Calculated %: C 71.30; H 12.88.

Ethyl ester of geranic acid (XXXVIII). A mixture of 13 g of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X), 20 ml of ether and 160 ml of 10% sulfuric acid was stirred for 1.5 hours at room temperature. The temperature of the reaction mass rose to 30°. The ether layer was separated, washed with water until neutral, dried with calcined magnesium sulfate and distilled to give 11.7 g (90%) of the ethyl ester of geranic acid (XXXVIII).

B.p. 68-71° (0.01 mm), $n^{20}D$ 1.4666, d^{20}_4 0.9145, MR 59.51; calc. 58.34.

Found %: C 73.18, 73.13; H 10.62, 10.52. $C_{12}H_{20}O_2$. Calculated %: C 73.41; H 10.20.

Hydrolysis of the ethyl ester of geranic acid with 10% methanolic solution fof potassium hydroxide gave geranic acid in 74% yield; b.p. 93-95° (0.03 mm), $n^{17.5}D$ 1.4780.

Found %: C 71.35, 71.38; H 9.29, 9.49. $C_{10}H_{16}O_2$. Calculated %: C 71.50; H 9.55.

Condensation of ethoxyacetylene with 2-methylhepta-2,4-dien-6-one. Dehydrocitral (XXXIV). 14.1 g (0.114 mole) of freshly distilled 2-methylhepta-2,4-dien-6-one (XXI) ($n^{20}D$ 1.5300) in 30 ml of absolute ether was added with stirring and cooling (ice and salt) in the course of an hour in a nitrogen stream to the ethoxyethynyl magnesium bromide prepared from 3.56 g of magnesium, 16.5 g (0.152 mole) of ethyl bromide and 10.8 g (0.154 mole) of ethoxyacetylene in 100 ml of absolute ether. The reaction mass was stirred for 1 hour at room temperature and for 35 minutes at 35°. After the usual working-up, the ethereal extract was dried with magnesium sulfate, and the ether was distilled off in a low vacuum in a nitrogen stream at room temperature. The residue was held in a 2 mm vacuum at 25-30° for 1.5 hours. The reaction product was a brownish-yellow oil, weight 20.9 g. A part of this (5.9 g) was distilled in vacuo in a nitrogen stream. 1.8 g of 2,6-dimethyl-8-ethoxyocta-2,4-dien-7-yn-6-ol (XXII) came over. The tarry residue after distillation weighed 3.8 g.

B.p. 83-93° (0.04-0.2 mm), $n^{20}D$ 1.5460, d^{20}_4 0.9699, MR 63.34; calc. 57.78.

Found %: C 73.78, 73.84; H 9.31, 9.21. $C_{12}H_{18}O_2$. Calculated %: C 74.20; H 9.28.

The carbinol (XXII) is an oily, yellow liquid which also decomposes on redistillation. Due to the impossibility of distilling the prepared product without decomposition, its content of carbinol (XXII) was determined by the Chugaev-Tserevitinov method (found 66%).

13.7 g of undistilled product, containing 9.07 g of carbinol (XXII), was hydrogenated in 20 ml of absolute ether in presence of 0.4 g of Pd catalyst. In the course of 2 hours the quantity of hydrogen absorbed was 1132 ml (1 mole) (22°, 739.5 mm). After the usual treatment with 3% sulfuric acid, the product was distilled in vacuo in a nitrogen stream to give the following fractions: 1st, b.p. 45-60° (0.11 mm), 0.45 g; 2nd, b.p. 65-84° (0.11 mm), 6.5 g; tarry residue 4.7 g.

The 2nd fraction was redistilled to give 4.5 g of dehydrocitral (XXXIV) in the form of a yellow liquid with a characteristic odor; b.p. 77-79° (0.23 mm), $n^{19}D$ 1.5681.

The semicarbazone melted at 204-205° after two recrystallizations from methanol; λ_{max} (in methanol), 332, 346 mμ.

Found %: N 20.63, 20.61. $C_{11}H_{17}ON_3$. Calculated %: N 20.28.

The 2,4-dinitrophenylhydrazone melted at 211-212° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 381, 397, 420 mμ.

Found %: N 16.98, 17.28. $C_{16}H_{18}O_4N_4$. Calculated %: N 16.98.

The above-described semicarbazone and 2,4-dinitrophenylhydrazone did not give a depression of melting point in admixture with the corresponding derivatives of citral obtained by polyenic condensation of dimethylacrolein under the influence of piperidine acetate.

Ethyl ester of dehydrogeranic acid (XLIV). Dehydrogeranic acid. An ethereal extract of 2,6-dimethyl-8-ethoxyocta-2,4-dien-7-yn-6-ol (XXII) was obtained by the above-described procedure from 2.98 g of magnesium, 14.7 g of ethyl bromide, 9 g of ethoxyacetylene and 11.85 g of methylheptadienone (XXI). To the solution was a added 130 ml of 10% sulfuric acid, and the mixture was stirred for 2 hours. After the usual treatment, the product was distilled in a nitrogen stream to give the following fractions: 1st, b.p. 60-67° (0.08 mm), 0.4 g; 2nd, b.p. 88-96° (0.08 mm), $n^{23}D$ 1.5485, 7.6 g; tarry residue 8.6 g.

Redistillation of the 2nd fraction gave 6.3 g of the ethyl ester of dehydrogeranic acid (XLIV) in the form of a greenish liquid; λ_{max} (in isooctane) 307 mμ.

B.p. 86-88° (0.02 mm), $n^{20}D$ 1.5560, d^{20}_4 0.9482, MR 65.89; calc. 57.87.

Found %: C 73.70, 73.94; H 9.39, 9.37. $C_{12}H_{18}O_2$. Calculated %: C 74.17; H 9.28.

Hydrolysis of ester (XLIV) with 2 N sodium hydroxide solution in a nitrogen atmosphere gave a 60% yield of yellow, crystalline dehydrogeranic acid with m.p. 182-183° (from ethyl acetate). The literature reports m.p. 185-186° [12]; λ_{max} (in isooctane) 307 mμ.

Found %: C 72.49, 72.63; H 8.52, 8.47. $C_{10}H_{14}O_2$. Calculated %: C 72.40; H 8.44.

Condensation of benzaldehyde with ethoxyacetylene. 10.2 g (0.096 mole) of benzaldehyde in 15 ml of absolute ether was added dropwise in a nitrogen stream, with stirring and cooling (ice and salt), to the ethoxyethynyl magnesium bromide prepared from 2.3 g of magnesium, 11 g (0.1 mole) of ethyl bromide, and 7 g (0.1 mole) of ethoxyacetylene in 80 ml of absolute ether. The mixture was stirred for 1 hour at room temperature and for 15 minutes at 35°. After the usual treatment the ethereal extract was divided into two halves. Ether was removed from one portion in vacuo. An attempt to distil the residue in high vacuum in a nitrogen stream led to exothermal decomposition of the substance; at a bath temperature of 140° and a vacuum of 0.02 mm, spontaneous decomposition started with evolution of gas and rise of temperature to 170°. To the second portion of the ether extract was added 135 ml of 10% sulfuric acid. The mixture was stirred for 1 hour and worked up as usual to give 8.4 g of ethyl cinnamate (XLV) with b.p. 83-84° (0.02 mm), $n^{20}D$ 1.5596. Tarry residue 4.2 g.

TABLE 4

Ethoxyethynyl Carbinols

Carbinol No.	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Found(%)		Calculated (%)	
				C	H	C	H
(VI)	64—65° (2)	1.4736	0.9590	71.43, 71.05	9.51, 9.44	71.40	9.52
(XII)	94—97 (0.02)	1.4684	0.9234	73.94, 73.88	10.55, 10.57	74.23	10.54
(XIV)	101—103 (0.1)	1.4680	0.9156	74.63, 74.85	10.82, 10.96	74.96	10.78
(XVI)	118—120 (1)	1.4653	0.9024	76.48, 76.51	11.16, 11.01	76.14	11.15
(XVIII)	116—118 (1)	1.4705	0.9147	75.28, 75.21	11.20, 11.16	75.54	11.10
(XX)	105—107 (0.5)	1.4817	1.0430	60.91, 60.83	8.02, 7.87	60.95	7.91

TABLE 5

Aldehydes

Aldehyde No.	Boiling point (pressure in mm)	2,4-Dinitrophenylhydrazones			
		melting point	λ_{max} (m μ) in isooctane	found N (%)	calc. N (%)
(XXVI)	37—38° (0.04)	140—141°	362, 370, 387	18.07, 18.25	18.20
(XXIX)	65—67 (0.01)	74—80	365	16.67, 16.58	16.20
(XXX)	77—80 (0.1)	148—150	365	15.48, 15.41	15.65
(XXXI)	83—85 (0.02)	140—142	255, 365	14.57, 14.63	14.50
		99.5—101	364	14.54, 14.78	
(XXXII)	79—82 (0.2)	157—158	365	14.90, 14.71	14.98
(XXXIII)	80—84 (0.25)	131—133	365, 379	16.01, 15.78	15.97
		102—104	365, 379	15.97, 15.81	

Hydrolysis of ester (XLV) gave cinnamic acid with m.p. 133-135°.

Condensation of ethoxyacetylene with β,β-dimethylacrolein. 23.5 g of freshly distilled β,β-dimethylacrolein in 25 ml of absolute ether was added to the ethoxyethynyl magnesium bromide prepared from 6.1 g of magnesium, 28 g of ethyl bromide and 18 g of ethoxyacetylene in 150 ml of absolute ether. The reaction mass was stirred for 2.5 hours at room temperature and worked-up in the usual manner. The ethereal extract was divided into two halves. The ether was removed from the first part in vacuo at room temperature in a nitrogen stream. Removal of the ether was at once followed by spontaneous decomposition accompanied by rise of temperature to 180°, by evolution of gas and by resinification. 225 ml of 10% sulfuric acid was added to the second portion of ethereal extract. The mixture was stirred for 45 minutes and worked-up in the usual manner.

Vacuum distillation in a nitrogen stream gave 5.3 g of the ethyl ester of δ-methylsorbic acid (XLVII). The tarry residue after distillation weighed 6.5 g.

B.p. 49-52° (0.05 mm), $n^{25}D$ 1.4980, $n^{20}D$ 1.5004, d^{20}_4 0.9432, MR 48.07; calc. 44.48.

Ester (XLVII) is a colorless liquid which turns yellow on standing. Hydrolysis of the ester with a methanolic solution of sodium hydroxide gave a 90% yield of δ-methylsorbic acid with m.p. 109-110° [12].

TABLE 6

Ester No.	Boiling point (pressure in mm)	n^{20}_D	d^{20}_4	Found (%)		Calculated (%)	
				C	H	C	H
(XXXV)	59—60°(27)	1.4375	0.9200				
(XXXVII)	78—80 (80)	1.4827	0.9036	71.69, 71.75	9.30, 9.44	71.40	9.52
(XXXIX)	76—79 (0.02)	1.4671	0.9107	74.27, 74.24	10.60, 10.54	74.23	10.54
(XL)	81—83 (0.05)	1.4669	0.9059	75.25, 75.39	10.81, 11.00	74.96	10.78
(XLI)	93—94 (0.13)	1.4652	0.8971	76.47, 76.55	11.10, 11.25	76.14	11.15
(XLII)	72—74 (0.01)	1.4684	0.9022	75.73, 75.34	11.35, 11.28	75.54	11.10
(XLVI)	83—85 (0.25)	1.4349	0.8986	—	—	—	—
(XLIII)	85—86 (0.2)	1.4778	1.0280	60.96, 61.29	7.72, 7.62	60.95	7.91

The other compounds listed in Tables 1-3 were prepared in similar fashion. Their constants and analyses are presented in Tables 4-6.

SUMMARY

The procedure for preparation of ethoxyacetylene was improved and its condensation with various aldehydes and ketones was described. The resulting ethoxyethynyl carbinols were converted in high yields into the corresponding α,β-unsaturated aldehydes and esters.

Received January 12, 1957

Moscow Institute of Fine Chemical
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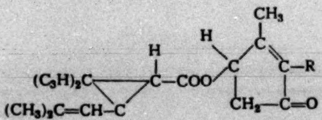
*Original Russian pagination. See C. B. translation.

ORGANIC INSECTOFUNGICIDES

XXX. SYNTHESIS OF SOME DERIVATIVES OF 1-METHYLCYCLOPENTANEDIONE-2,3

N. N. Mel'nikov and K. D. Shvetsova-Shilovskaia

As is known, various pyrethrin preparations, which are practically harmless to warm-blooded animals and man but rapidly affect many harmful insects, have been quite widely used as active contact insecticides. The active principles of these preparations are esters of chrysanthemic acids with 1-methyl-2-alkyl-5-hydroxycyclopenten-1-ones-3 (I), known as pyrethrin-1, pyrethrin-2, cinerin-1 and cinerin-2. However, the preparation of large quantities of these compounds is extremely complicated; the preparation of alletrin and furetrin is somewhat less complicated but they too are very expensive [1].

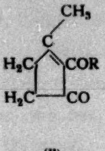


(I)

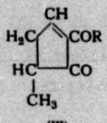
$R = CH_2CH = CHCH = CH_2$ pyrethrin-1

$R = CH_2CH = CHCH_3$ cinerin-1

In connection with the above, attempts at synthesizing and studying the insecticidal properties of simpler compounds, similar in structure to pyrethrins and cinarins, are continuing. With the aim of finding new active insecticides, we synthesized a series of new esters of the enol of 1-methylcyclopentanedione-2,3, as this diketone is readily available. The esters of 1-methylcyclopentenolone were synthesized by reacting 1-methylcyclopentanedione-2,3 with the acid chlorides of appropriate acids in the presence of potassium carbonate with prolonged heating in hydrophobic organic solvent. Considering the behavior of some cyclic ketones, one would expect that the main reaction products in our case would be compounds with the general formula (II) [2] although traces of compounds with the general formula (III) are also possible.



(II)



(III)

The compounds synthesized, and their properties, are given in the table.

Of the compounds we synthesized, only the esters of thiophosphoric acid had insecticidal activity while the esters of carbamic, acetic, butyric and carbonic acids were inactive.

EXPERIMENTAL

We prepared esters of the enol of 1-methylcyclopentanediene-2,3 by the following method; a solution of the diketone in benzene, dichloroethane or another solvent of the same type was placed in a flask with a reflux condenser, a mechanical stirrer and a dropping funnel; finely powdered, dry potassium carbonate was added and the acid chloride introduced through the dropping funnel, with vigorous stirring and heating. Heating was continued for 8 to 20 hours. After the reaction, the precipitate was filtered and the solvent distilled off. After removal of the solvent, the product obtained was fractionated in vacuum. In most cases the yields did not exceed 50-60%. The compounds synthesized and their properties are listed in the table.

Properties of Compounds (II)

R	Melting point	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Analysis (%)			
					Found		Calculated	
					C	H	C	H
$(CH_3)_2NCO$ . . .	58—59.5°	108 (0.2)	—	—	59.26, 59.62	7.55, 7.49	59.0	7.16
$(C_2H_5)_2NCO$ . . .	36—38	115—122 (0.3)	—	—	62.85, 62.11	8.42, 8.30	62.54	8.11
CH_3OCO	43—45	96—97 (0.25)	—	—	57.4, 57.13	6.40, 6.46	56.4	5.88
C_2H_5OCO	53—55	103—107 (0.15)	—	—	59.09, 59.46	6.82, 6.68	68.60	6.56
CH_3CO	—	75 (0.075)	—	1.4859	61.66, 61.51	6.83, 6.84	62.30	6.53
C_3H_7CO	—	82.5—85 (0.1)	—	1.4739	65.18, 65.19	7.78, 7.89	65.85	7.74
					% P		% P	
$(CH_3O)_2PS$ . . .	—	116—117 (0.2)	1.2562	1.5155	12.51, 12.71		13.10	
$\left.\begin{matrix}CH_3O\\C_2H_5O\end{matrix}\right>PS$ . . .	—	125—127 (0.1)	1.2254	1.5060	12.50, 12.08		12.38	
$(C_2H_5O)_2PS$ . . .	—	126—128 (0.2)	1.1715	1.5025	11.72, 11.73		11.75	

SUMMARY

In order to find new active insecticides we synthesized a series of esters of the enol of 1-methylcyclopentanedione-2,3 that had not been described in the literature. On studying the insecticidal properties, we found that the esters of acetic, butyric, carbamic and methoxy- and ethoxycarbonic acids were practically inactive. The esters of dialkoxythiophosphoric acid were active.

Received January 16, 1957

Scientific Institute of Fertilizers and
Insectofungicides

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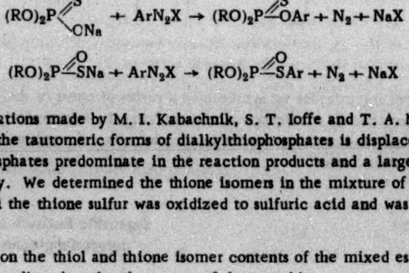
ORGANIC INSECTOFUNGICIDES

XXXI. A NEW METHOD OF PREPARING MIXED ESTERS OF THIOPHOSPHORIC ACID

N. N. Mel'nikov, Ia. A. Mandel'baum and V. I. Lomakina

Recently, a new method was developed in our laboratory for preparing mixed esters of dithiophosphoric acid [1] by reacting aromatic diazo compounds with salts of dialkyldithiophosphoric acid. This method allows the preparation of mixed aliphatic-aromatic esters of dithiophosphoric acid, containing the most varied functional groups in the aromatic radical. It seemed interesting to find out if this method could be applied to the synthesis of esters not only of dithiophosphoric acid, but also mixed esters of monothiophosphoric acid, which are likewise valuable as active insecticides against various pests [2]. A study of the reaction of aromatic diazo compounds with salts of dialkylthiophosphoric acid is especially interesting in connection with the presence of tautomerism and the dual reactivity of the latter [3].

As a result of experiments carried out, it was established that the reaction of aromatic diazo compounds with dialkylthiophosphoric acid salts in an acidic aqueous solution gave a 50% yield of mixed esters of thiophosphoric acid. Under these conditions a mixture of thiol and thione isomers was formed, i.e., the dialkylthiophosphoric acid salts reacted in both of the tautomeric forms and this can be represented by the following general schemes



$$(RO)_2P\overset{S}{\underset{ONa}{<}} + ArN_2X \rightarrow (RO)_2P\overset{S}{=}OAr + N_2 + NaX$$

$$(RO)_2P\overset{O}{=}SNa + ArN_2X \rightarrow (RO)_2P\overset{O}{=}SAr + N_2 + NaX$$

Regarding the observations made by M. I. Kabachnik, S. T. Ioffe and T. A. Mastriukova [4], in our investigations the equilibrium of the tautomeric forms of dialkylthiophosphates is displaced toward the thiol form, as O,O-dialkyl-S-arylthiophosphates predominate in the reaction products and a large amount of the thione isomer is obtained in one case only. We determined the thione isomers in the mixture of esters by oxidation with 55% nitric acid. In this case all the thione sulfur was oxidized to sulfuric acid and was readily determined in the form of barium sulfate.

The results obtained on the thiol and thione isomer contents of the mixed esters of thiophosphoric acid show that not only the reaction medium but also the nature of the attacking agent quantitatively affects the composition of the mixture.

EXPERIMENTAL

We prepared the sodium diethyl thiophosphate in benzene, by A. E. Arbuzov's method, and obtained an 80% yield. The m.p. was 194°. Salts of this quality was used for all experiments on the preparation of mixed esters of thiophosphoric acid.

Preparation of mixed esters of thiophosphoric acid. To illustrate the conditions we used for reacting aryldiazonium salts with sodium diethylthiophosphate, we will describe the preparation of diethylphenylthiophosphate. A solution of phenyldiazonium chloride was prepared in the usual way from 9.5 g of aniline, 25 ml of concentrated hydrochloric acid and 6.9 g of sodium nitrite (in 25 ml of water). Air was passed through the solution obtained for

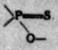
2 hours (at 0°) to remove the residual nitrous acid. Then a solution of 19.2 g of sodium diethylthiophosphate in 50 ml of water and 2 g of copper sulfate were added to the solution of phenyldiazonium chloride.

After the addition of the copper sulfate, the reaction mixture was gradually heated to 50° and kept at this temperature until the evolution of nitrogen ceased (this required about 1 hour). The mixture was cooled, the oil liberated extracted with ether, the ether solution washed with water and dried over anhydrous calcium chloride and, after removal of the ether, the product obtained was distilled several times in vacuum. After two distillations, a fraction with b.p. 117-123° (0.7 mm) was collected. The yield was about 8.1 g (31%), d^{20}_4 1.1633, $n^{20}D$ 1.5172.

Found %: P 12.1, 12.3; S 12.70, 12.75; C 46.77, 46.83; H 6.70, 6.66. $C_{10}H_{15}O_3PS$. Calculated %: P 12.16; S 13.10; C 46.34; H 6.09.

The other mixed esters of thiophosphoric acid were prepared under exactly the same conditions. The compounds we prepared, and their properties, are listed in the table.

Properties of Mixed Esters of Thiophosphoric Acid $(C_2H_5O)_2PSOAr$

Ar	B.p. (pressure in mm)	d^{20}_4	n^{20}_D	Isomer content (%)		Analysis (%)			
						Found		Calc.	
						P	S	P	S
o-$CH_3C_6H_4$ . .	92—96° (0.3)	1.1319	1.4930	37	63	12.30, 12.30	12.70, 12.80	11.92	12.3
m-$CH_3C_6H_4$ . .	75—80 (0.12)	1.1253	1.5094	44	56	11.32, 11.63	11.60, 11.70	11.92	12.0
p-$CH_3C_6H_4$ . .	127—130 (0.2—0.3)	1.1713	1.5129	55	45	11.73, 11.71	11.80, 11.90	11.92	12.3
p-ClC_6H_4 . . .	119—123 (0.3)	1.2568	1.5298	37	63	10.80, 10.90	12.8,* 12.9	11.00	12.5
p-$CH_3OC_6H_4$.	160—166° (0.6)	1.1547	1.5705	86	14	10.7	—	11.20	–

Determination of thione isomer content. As already indicated above, the thione isomer in the mixture of isomers was determined by oxidation with 55% nitric acid. A sample (0.1-0.2 g) of the preparation was heated with 30-50 ml of 55% nitric acid for 4-5 hours in a water bath with continuous agitation. When a completely clear solution had been obtained, the reaction mixture was diluted with water and the sulfuric acid formed precipitated in the usual way as barium sulfate. (If a turbid solution was obtained on dilution with water, indicating that the oxidation was incomplete, a new sample was taken and the experiment repeated.) Each determination was performed at least twice. For the diethylphenylthiophosphate we obtained a thione sulfur content of 3.08 and 2.81%, indicating a content of 23% O,O-diethyl-O-phenylthiophosphate and 77% O,O-diethyl-S-phenylthiophosphate. Data on the determination of the isomer content of the other esters of thiophosphoric acid are given in the table.

SUMMARY

The reaction of sodium diethylthiophosphate with aromatic diazo compounds was studied. It was shown that sodium diethylthiophosphate reacts with aryldiazonium salts in two tautomeric forms to give mixed esters of thiophosphoric acid.

Received January 16, 1957

Scientific Institute of Fertilizers and
Insectofungicides

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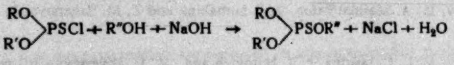
ORGANIC INSECTOFUNGICIDES

XXXII. SYNTHESIS OF SOME MIXED ESTERS OF THIOPHOSPHORIC ACID

Ia. A. Mandel'baum, N. N. Mel'nikov and N. I. Petrova

In 1949 a method was developed in our laboratory for preparing esters of thiophosphoric acid by reacting phosphorus thiotrichloride with alcohols in the presence of caustic alkalis [1]. This method was recently extended to cover the preparation of mixed aliphatic esters of chlorothiophosphoric acid [2]. In order to assess the possibility of using this method for the synthesis of mixed esters of thiophosphoric acid of the aliphatic series, we studied the reaction of mixed dialkylchlorothiophosphates with methyl and ethyl alcohols in the presence of sodium hydroxide. As a result of the experiments, it was established that dialkylchlorothiophosphates react with alcohols in the presence of sodium hydroxide to give good yields of the corresponding trialkylthiophosphates. This reaction may be represented by the following general scheme



$$\begin{smallmatrix}RO\\R'O\end{smallmatrix}\!\!>PSCl + R''OH + NaOH \rightarrow \begin{smallmatrix}RO\\R'O\end{smallmatrix}\!\!>PSOR'' + NaCl + H_2O$$

The compounds we obtained, and their properties, are listed in the table. Almost all the compounds we synthesized have not been described in the literature.

EXPERIMENTAL

Preparation of dimethylalkylthiophosphates. With cooling and vigorous stirring, 45 ml of a solution of sodium hydroxide in 80% methyl alcohol (containing 4.95 g of sodium hydroxide) was added to 0.1 mole of methylalkyl-

Properties of Mixed Esters of Thiophosphoric Acid

Formula	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	P analysis (in %)	
					Found	Calc.
$(CH_3O)_2PSOC_3H_7$-iso	90	79—80° (12)	1.1031	1.4540	16.01, 16.10	16.81
n-$C_4H_9OPS(OCH_3)_2$	84	89—91 (10)	1.0939	1.4561	14.95, 15.10	15.63
iso-$C_5H_{11}OPS(OCH_3)_2$	91.5	96—99 (10)	1.0801	1.4560	14.50, 14.70	14.44
$C_3H_7OPS\begin{smallmatrix}OCH_3\\OC_2H_5\end{smallmatrix}$	74.5	58—61 (0.3)	1.1224	1.4540	16.20, 16.40	15.63
$C_4H_9OPS\begin{smallmatrix}OCH_3\\OC_2H_5\end{smallmatrix}$	76	60—64 (0.3)	1.0625	1.4490	14.80, 15.10	14.44
iso-$C_4H_9OPS\begin{smallmatrix}OCH_3\\OC_2H_5\end{smallmatrix}$	80	64—67 (0.3)	1.0540	1.4470	14.90, 15.10	14.44
iso-$C_5H_{11}OPS\begin{smallmatrix}OCH_3\\OC_2H_5\end{smallmatrix}$	64	70—72 (0.25)	1.0645	1.4560	14.20, 14.10	13.45

chlorothiophosphate. During the addition of the sodium hydroxide the temperature was not allowed to rise above 10°. When all the sodium hydroxide had been added, the reaction mixture was stirred at 20° for 2 hours. Then the reaction mixture was diluted with water and the oil which formed was separated, washed with water, dried over anhydrous calcium chloride and vacuum distilled. The distilled preparation was analyzed for phosphorus by a photocolorimetric method [3].

2. Preparation of methylethylalkylthiophosphates. With vigorous stirring and cooling to 0°, 5 g of powdered sodium hydroxide was gradually added to a solution of 0.1 mole of methylalkylchlorothiophosphate in 20 ml of absolute ethyl alcohol. The reaction mixture was then stirred at 20° for 2 hours. After the reaction the mixture was treated with water and the oil was separated, washed with a small amount of water, dried over anhydrous calcium chloride and fractionated in vacuum. The purified preparation was analyzed. The compounds we prepared and their properties are listed in the table.

SUMMARY

A new and simple method was developed for preparing mixed esters of thiophosphoric acid giving 70-94% yields, by reacting dialkylchlorothiophosphates with alcohols in the presence of sodium hydroxide. Most of the compounds synthesized have not been described in the literature.

Received January 16, 1957

Scientific Institute of Fertilizers and Insectofungicides

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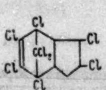
* Original Russian pagination. See C. B. translation.

ORGANIC INSECTOFUNGICIDES

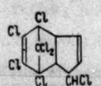
XXXIII. THE SYNTHESIS OF SOME DERIVATIVES OF 4,7-ENDOMETHYLENETETRAHYDROINDAN

S. S. Kukalenko, N. N. Mel'nikov, T. I. Naryshkina and N. I. Shuikin

In recent years the chloro derivatives of hydrocarbons, synthesized by a diene reaction from hexachlorocyclopentadiene and various unsaturated compounds [1-3] have been quite widely used in agriculture. The simplest insecticides of this group of compounds are 1,2,4,5,6,7,8,8-octachloro-4,7-endomethylene-3a,4,7,7a-hexahydroindan (I) and 1,4,5,6,7,8,8-heptachloro-4,7- endomethylene-3a,4,7,7a-tetrahydroindan (II), which are known under the trade names of "chlordan" and "heptachlorine."


Cl
Cl
CCl₂
Cl
Cl
Cl
Cl

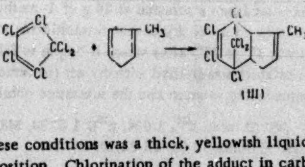
(I)


Cl
Cl
CCl₂
Cl
Cl
CHCl

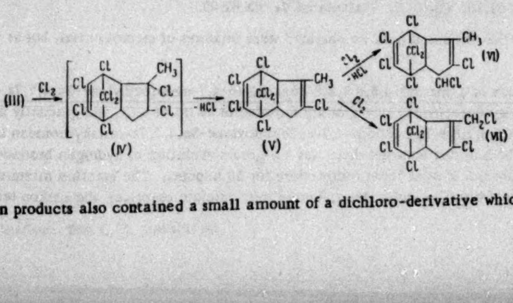
(II)

In spite of the fact that these compounds are produced on a large industrial scale, even their closest homologs have not been studied until now. A study of chlordan and heptachlorine homologs undoubtedly would be valuable for investigating the relation of insecticide activity to structure in this series of compounds.

In connection with the above, we undertook a study of the adduct of hexachlorocyclopentadiene with 3-methylcyclopentadiene-2,4. The adduct of hexachlorocyclopentadiene with methylcyclopentadiene was prepared by heating a mixture of the starting substances for a short time at 85-105°. This reaction may be represented by the following scheme


Cl
Cl
CCl₂
Cl
Cl
+
CH₃
Cl
Cl
CCl₂
Cl
Cl
CH₃
(III)

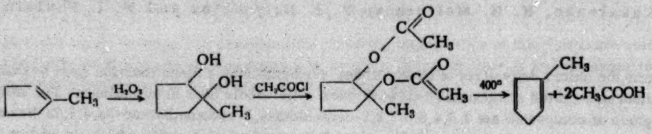
The adduct obtained under these conditions was a thick, yellowish liquid with a slight, unpleasant smell which distilled in vacuum without decomposition. Chlorination of the adduct in carbon tetrachloride with gaseous chlorine gave a monochloro derivative as the main product, and its formation may be represented by the following scheme


(III)
Cl₂
Cl
CH₃
Cl
CCl₂
Cl
Cl
Cl
Cl
(IV)
-HCl
Cl
CH₃
Cl
CCl₂
Cl
Cl
Cl
(V)
Cl₂
-HCl
Cl
CH₃
Cl
CCl₂
Cl
Cl
Cl
CHCl
(VI)
Cl₂
Cl
CH₂Cl
Cl
CCl₂
Cl
Cl
Cl
(VII)

The chlorination products also contained a small amount of a dichloro-derivative which could be assigned the structure (IV), (VI) or (VII), though the most probable structure would correspond to formulas (IV) or (VI), as may be deduced by comparison with the behavior of the adduct of hexachlorocyclopentadiene with cyclopentadiene (I). Bromination of the adduct apparently proceeded by a similar scheme as the main product of this reaction was a monobromo-derivative. It is interesting to note that all the derivatives we synthesized have a weaker insecticidal effect than chlordan and much weaker than heptachlorine.

EXPERIMENTAL

1. Synthesis of methylcyclopentadiene. The starting methylcyclopentadiene was synthesized by two methods. One part of it was prepared by catalytic dehydrocyclization [4] of 3-methylpentadene -1,3 (b.p. 76-77°, $n^{20}D$ 1.4460, d^{20}_4 0.7296), which, in its turn, was prepared by dehydration of methylethylvinylcarbinol [5]. The bulk of the methylcyclopentadiene was prepared by another method, namely, pyrolysis of the diacetate of 1-methylcyclopentanediol-1,2, prepared from the corresponding glycol and acetyl chloride by the scheme



The 40 g of methylcyclopentadiene prepared was mainly the β-isomer [4].

B.p. 73-74° (749 mm), $n^{20}D$ 1.4510, d^{20}_4 0.8192.

Found MR_D 26.31. C_6H_8. Calculated: 26.77.

2. Reaction of hexachlorocyclopentadiene with 3-methylcyclopentadiene-2,4. 136.5 g of hexachlorocyclopentadiene was placed in a flask with a reflux condenser, a mechanical stirrer and a dropping funnel and heated to 85° and then 40 g of 3-methylcyclopentadiene-2,4 was gradually added to it from the dropping funnel. The temperature of the reaction mixture rose to 104°. When all the methylcyclopentadiene had been added, the reaction mixture was kept at 100° for 30 minutes and then fractionated in vacuum. We obtained 100 g of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3,4,7,7a-tetrahydroindan.

B.p. 144-145° (4 mm), d^{20}_4 1.5251, $n^{20}D$ 1.5610, MR_D 74.98; calculated 74.66.

Found %: C 38.13, 37.90; H 2.83, 2.60; Cl 60.94. $C_{11}H_8Cl_6$. Calculated %: C 37.39; H 2.26; Cl 60.34.

3. Chlorination of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan. A stream of dry, gaseous chlorine was passed into a solution of 30 g of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan in 75 ml of dry carbon tetrachloride at room temperature for 50 minutes. During this, the temperature rose from 17° to 35°, after which it began to fall indicating the end of the reaction. After the chlorination the reaction mixture was flushed with dry air (to remove excess chlorine and hydrogen chloride). Then the solvent was removed in vacuum and the substance obtained was fractionated.

1st fraction (20 g), b.p. 150-153° (2 mm), d^{20}_4 1.604, $n^{20}D$ 1.5720, MR_D 79.49; calc. 79.53.
Found %: Cl 64.42. $C_{11}H_7Cl_7$. Calculated %: Cl 64.10.

2nd fraction (10 g), b.p. 167-170° (2 mm), d^{20}_4 1.6460, $n^{20}D$ 1.5764, MR_D 85.25; calc. 84.87.

Found %: Cl 67.38, $C_{11}H_6Cl_8$. Calculated %: Cl 67.00.

It is possible that the substances we obtained were mixtures of stereoisomers, but as yet we have not separated them.

4. Bromination of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan. With cooling to 0° and vigorous stirring, 12.1 g of dry bromine in 50 ml of CCl_4 was gradually added to a solution of 27 g of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan in 50 ml of carbon tetrachloride. During the bromine addition there was a vigorous evolution of hydrogen bromide. At the end of the reaction, the mixture was kept at room temperature for 30 minutes. The reaction mixture was then washed with an aqueous solution of bisulfite and water and dried over calcium chloride; the carbon tetrachloride was distilled

off and the product fractionated in vacuum. The yield was 19 g.

B.p. 167-170° (4 mm), d^{20}_4 1.7406, $n^{20}D$ 1.5880, MR_D 82.99; calc. 82.43.

Found %: C 31.40, 31.67; H 1.75, 1.86. $C_{11}H_7Cl_6Br$. Calculated %: C 30.56; H 1.62.

SUMMARY

It was shown that hexachlorocyclopentadiene reacted with 3-methylcyclopentadiene-2,4 to give an adduct with the composition $C_{11}H_8Cl_6$, and chlorination of it gave mono- and dichloro derivatives. Bromination of the adduct gave a monobromo derivative. None of the compounds synthesized have been described in the literature and are weaker insecticides than chlordan.

Received January 16, 1957

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Sciences USSR

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*Original Russian pagination. See C. B. translation.

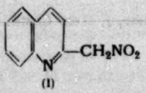
SOME REACTIONS OF 2-NITROMETHYLQUINOLINE

I. SALT FORMATION AND THE ACTION OF HALOGENS

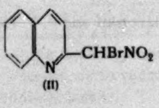
L. Zalukaev and E. Vanags

2-Nitromethylquinoline, which was described previously [1, 2] (I) and has now become a readily accessible compound, was investigated by us from the chemical point of view in more detail. The present work presents data on salt formation and the action of halogens on this nitro compound, which is interesting in many ways.

As could be expected, the methylene group in 2-nitromethylquinoline has an extremely labile hydrogen atom and is highly reactive. The substance dissolved very readily in alkalis to form salts. The potassium salt and even the ammonium salt could be prepared without any special difficulties. The hydrogen atoms in the side chain were substituted by chlorine and bromine at room temperature with exceptional ease to give the corresponding mono- and dihalo derivatives.



(I)

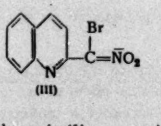


(II)

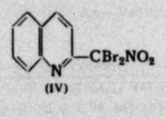
The preparation of bromonitromethylquinoline was partly described previously [1]. This substance was obtained by treating an acetic acid solution of 2-nitromethylquinoline with bromine in the presence of a small amount of sulfuric acid. On the basis of its high stability to boiling alcoholic potassium hydroxide, a hypothesis was put forward that the halogen atom was aromatically bound. However, further investigations showed that the substance should be assigned formula (II).

Three facts confirm this. Firstly, the substance dissolved readily in alkalis and is recovered unchanged on acidification. Secondly, the substance readily loses a bromine atom when treated with benzoyl chloride. Thirdly, the UV spectra of the monohalo derivatives are similiar in character (Fig. 1) to the spectrum of 2-nitromethylquinoline, whose structure was proved to be (I). This gives grounds for assigning formula (II) to the substance and for noting its exceptional stability to alkalis.

It is probable that the bromine-carbon bond in salts (III) of the nitronic acid is similar in character to an aromatic one. This apparently, explains the capacity of ammonia (for which the capacity for forming nitronic salts is less characteristic) for eliminating a bromine atom from substance (II).



(III)



(IV)

The monochloro derivatives have similiar properties and, in particular, when treated with benzoyl chloride give the same product as monobromo derivatives.

The structure of the dibromo derivative (IV) was confirmed, on the one hand, by its insolubility in alkalis and, on the other, by its relatively easy conversion to the monobromo derivative. In addition, a comparison of UV spectra (Fig. 2) and solubilities in strong acids also support structure (IV).

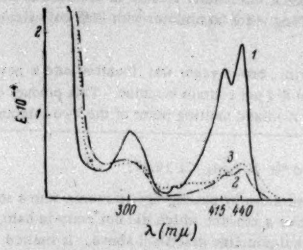


Fig. 1. UV spectra of quinolylnitromethane and its monohalo derivatives. 1) Quinolylnitromethane; 2) monobromoquinolylnitromethane; 3) monochloroquinolylnitromethane.

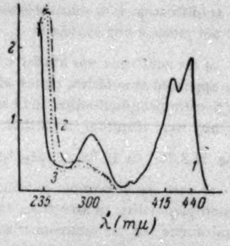


Fig. 2. UV spectra of quinolylnitromethane and its dihalo derivatives. 1) Quinolylnitromethane; 2) dibromoquinolylnitromethane, 3) dichloroquinolylnitromethane.

The situation is similar for 2-dichloronitromethylquinoline. The fact should be noted that chlorine replaced the bromine atom readily in the monobromo derivative to form the dichloro derivative.

The introduction of halogens into the nitromethyl group strongly decreased the basic properties of the quinoline ring as the halo derivatives of 2-nitromethylquinoline are very weak bases and are insoluble in dilute acids.

EXPERIMENTAL

Salts of 2-Nitromethylquinoline

Potassium salt. 1 g of the nitro compound was boiled for 10 minutes on a water bath with 10 ml of an alcohol solution of potassium hydroxide; the 2-nitromethylquinoline was thus converted into a salt. The mixture was cooled and the yellow precipitate separated and recrystallized from alcohol. We obtained 0.95 g of the substance.

Found %: N 12.55; K 16.85. $C_{10}H_7O_2N_2K$. Calculated %: N 12.39; K 17.26.

The salt was readily soluble in water; acidification with acetic acid liberated 2-nitromethylquinoline with m.p. 122-123°.

Ammonium salt. 70 ml of anhydrous alcohol was poured onto 2 g of the nitro derivative and dry gaseous ammonia passed through the mixture for 1 hour. After standing for 5 hours, the precipitate was sucked off and washed with alcohol. We obtained 1.85 g of the ammonium salt with m.p. 136° (decomp.). The salt could be recrystallized from alcohol, but the smell of ammonia was detected. Due to the unusual ease with which the salt was hydrolyzed, data on the nitrogen content were always low.

Found %: N 17.54. $C_{10}H_{11}O_2N_3$. Calculated %: N 20.48.

Acidification of an aqueous solution of the salt liberated the original 2-nitromethylquinoline. If the latter was treated with a methanol solution of picric acid a yellow picrate with m.p. 154-155° (decomp.) was precipitated. Recrystallization from alcohol did not change the melting point.

Found %: N 17.24. $C_{16}H_{11}O_9N_5$. Calculated %: N 16.79.

Upon reaction of the ammonium salt with liquid alkali, ammonia was produced.

Halogen Derivatives of 2-Nitromethylquinoline

2-Bromonitromethylquinoline [1]. 5 g of 2-nitromethylquinoline was dissolved in 50 ml of glacial acetic acid at room temperature and the solution treated with 2 ml of concentrated sulfuric acid and a solution of bromine in glacial acetic acid. After 5 minutes agitation and subsequent dilution with water, a yellow precipitate formed, which was filtered off, washed with water and recrystallized from alcohol after being dried. We obtained 4.5 g of 2-bromonitromethylquinoline with m.p. 122-123°. The substance was readily soluble in alkalis and was liberated unchanged by acidification with dilute acetic acid. Even boiling it for 30 minutes with 20% potassium hydroxide in alcohol did not produce any change in it.

If some of the substance was heated with benzoyl chloride, brown vapor was liberated and a new product formed, which appeared as colorless plates with m.p. 154° and did not contain bromine. This product could be obtained from 2-nitromethylquinoline and benzoyl chloride. A mixed melting point of the two substances was not depressed and they were identical in all their properties.

Found %: N 8.76; Cl 10.98. $C_{17}H_{13}O_3N_2Cl$. Calculated %: N 8.54; Cl 10.67.

In only one case was it possible to eliminate the bromine atom by passing dry ammonia into a solution of 2-bromonitromethylquinoline in anhydrous ethanol and this gave a product which did not contain halogen. By all the data, the substance was the ammonium salt of 2-nitromethylquinoline described above. It melted at 131-132° and partially lost ammonia during recrystallization from alcohol, but gave more satisfactory nitrogen analysis data before recrystallization.

Found %: N 19.19. $C_{10}H_{11}O_2N_3$. Calculated %: N 20.48.

2-Dibromonitromethylquinoline. One of us described 2-dibromonitromethylquinoline previously [1]. We present data proving its structure.

1 g of 2-dibromonitromethylquinoline was mixed with 30 ml of ethanol and then a stream of dry ammonia passed into the solution. As a result, we obtained the monobromo derivative described above with m.p. 122-123°, which was not depressed by admixture with the authentic product. The 2-dibromonitromethylquinoline was quite readily soluble in concentrated hydrochloric acid and reprecipitated unchanged by dilution with water.

2-Chloronitromethylquinoline. 2 g of 2-nitromethylquinoline was dissolved in 20 ml of glacial acetic acid at room temperature and then a saturated solution of chlorine in the same solvent added. A bright yellow precipitate formed on dilution with water. Recrystallization from glacial acetic acid yielded 0.35 g of yellow needles with m.p. 128-129°.

Found %: N 12.40; Cl 15.37. $C_{10}H_7O_2N_2Cl$. Calculated %: N 12.61; Cl 15.76.

With benzoyl chloride the substance gave a product with m.p. 154°, which was not depressed by admixture with the product from benzoylation of 2-nitromethylquinoline.

2-Dichloronitromethylquinoline. 3 g of 2-nitromethylquinoline was dissolved in 40 ml of glacial acetic acid and a stream of chlorine passed into the solution for 15 minutes. At first the dark yellow solution became almost colorless. The light precipitate, which formed after considerable dilution of the mixture with water, was carefully washed with water and dried. After recrystallization from alcohol, the colorless plates had m.p. 70-72°. The yield was 2.25 g (55%).

Found %: N 11.22; Cl 26.11. $C_{10}H_6O_2N_2Cl_2$. Calculated %: N 10.94; Cl 27.35.

The dichloro derivative did not react with aqueous alkali, but heating on a water bath with a 10% alcohol solution of KOH eliminated one atom of chlorine to give the monochloro derivative. 2-Dichloronitromethylquinoline dissolved in concentrated hydrochloric acid and was precipitated unchanged on dilution of the solution with water.

Action of chlorine on 2-bromonitromethylquinoline. 1 g of the monobromo derivative was treated with a solution of 0.26 g of chlorine in 20 ml of glacial acetic acid. Dilution with water gave a precipitate which weighed 0.9 g and had m.p. 68-70° after drying. The m.p. was 71-72° after the material had been recrystallized from alcohol. The melting point was not depressed by admixture with authentic 2-dichloronitromethylquinoline.

Found %: N 10.92. $C_{10}H_6O_2N_2Cl_2$. Calculated %: N 10.94.

SUMMARY

The salts and 2-halo derivatives of 2-nitromethylquinoline were prepared.

Received January 14, 1957

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*Original Russian pagination. See C. B. translation.

VINYLATION OF HYDROBENZOIN. I.

B. I. Mikhant'ev and L. P. Pavlov

Vinyl ethers are mainly prepared by the method of A. E. Favorskii and M. F. Shostakovskii [1]. This method is widely used in the Soviet Union and, with certain modifications, abroad [2]. M. F. Shostakovskii et al., [3] and other authors [4] describe the vinylation of polyatomic aliphatic alcohols with acetylene. The vinylation of aliphatic-aromatic and aromatic alcohols with several hydroxyls has not been examined so well.

We investigated the direct vinylation of hydrobenzoin and obtained its full vinyl ether — meso-α,α'-divinyldioxydibenzyl.

EXPERIMENTAL

Preparation of meso-α,α'-divinyldioxydibenzyl. 30 g of hydrobenzoin [5], 300 ml of dioxan and 6 g of potassium hydroxide were placed in a 1 liter rotating autoclave. The acetylene pressure was 15 atm (20°), the vinylation time at 130-135°, 6 hours and the maximum pressure 60 atm. The reaction mixture, which was a brown liquid, was filtered and distilled. We collected a fraction with b.p. 140-165° at 3-4 mm (weight 26 g), which was a constant boiling mixture and deposited fine crystals of the divinyl ether of hydrobenzoin on standing. These were separated and washed with alcohol several times. The yield was 6.4 g (17.1%). After two recrystallizations from alcohol, the melting point was 81-81.6°; the substance distilled at 139-139.5° (1.5 mm) with slight decomposition. The substance formed colorless needles, which were difficultly soluble in cold, but readily soluble in hot alcohol and also in ether, benzene and dioxan.

Found %: C 81.16, 81.01; H 6.59, 6.67. M 260.9. $C_{18}H_{18}O_2$. Calculated %: C 81.17; H 6.81. M 266.3.

Hydrolytic oximination and quantitative hydrogenation indicated the presence of two vinyl groups. The original alcohol was obtained by hydrolysis and a mixed melting point of this with hydrobenzoin was not depressed.

Preparation of meso-α,α'-diethoxydibenzyl. 3 g of the divinyl ether of hydrobenzoin was hydrogenated in 150 ml of alcohol in the presence of 0.3 g of Raney nickel. After separation of the nickel and evaporation of the solution, we obtained 2.7 g of crystals (88.6%). The product was recrystallized three times from alcohol and once from ether, when it had m.p. 66-66.3°; it formed colorless prisms; they were readily soluble in organic solvents and did not react with bromine water.

Found %: C 80.27, 80.03; H 8.26, 8.12. M 267.0. $C_{18}H_{22}O_2$. Calculated %: C 79.96; H 8.20. M 270.4.

Reaction with acetic acid (95%) in the presence of sulfuric acid at 100-110° and subsequent hydrolysis of the diacetate with alcoholic alkali yielded hydrobenzoin, proved by a mixed melting point.

SUMMARY

Hydrobenzoin and acetylene gave meso-α,α'-divinyldioxydibenzyl, which has not been described in the literature. Hydrogenation of it gave meso-α,α'-diethoxydibenzyl.

Received January 28, 1957

Voronezh State University

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* Original Russian pagination. See C. B. translation.

A STUDY OF THE EFFECT OF THE REAGENT'S CHARACTER ON THE DIRECTION OF O- AND C-SUBSTITUTION OF METAL DERIVATIVES OF A KETO-ENOL SYSTEM

V. A. Zagorevskii

The purpose of this work, carried out under the direction of A. N. Nesmeianov, was to obtain additional experimental data on the relation of the relative yields of O- and C-derivatives to the character of the reagent, reacting with metal derivatives of a keto-enol system. We investigated the action of a series of halogen derivatives on metal phenolates and β-naphtholates. Furthermore, we reacted sodium phenolate with sulfur trioxide, complexed with dioxan (dioxansulfur trioxide). The results of the main experiments are given in the table.

The Effect of the Reagent's Character on the Direction of O- and C-substitution

Exp. No.	Reagent	Metal derivative	Solvent; temperature	Derivative yields (in %)	
				O	C
1	p-Methoxybenzyl bromide	Sodium β-naphtholate	Acetone, 56-58°	47	24
2	Benzyl bromide	Sodium β-naphtholate	Acetone, 56-58	82	–
3	p-Nitrobenzyl bromide	Sodium β-naphtholate	Acetone, 56-58	87	–
4	Benzyl bromide	Sodium β-naphtholate	Acetone + benzene, 55-57	54	3
5	p-Nitrobenzyl bromide	Sodium β-naphtholate	Acetone + benzene, 55-57	85	Not more than 4
6	4-Bromo-1,3-dinitrobenzene	Sodium β-naphtholate	Boiling dioxan	67	–
7	Benzoyl chloride	Sodium β-naphtholate	Toluene, 100	90	–
8	Acetyl chloride	Dichloroaluminum phenolate	Boiling carbon disulfide	87	–
9	Triphenylmethyl chloride	Sodium phenolate	Boiling dioxan	22	27*
10	Tri-p-nitrophenylmethyl bromide	Sodium phenolate	Boiling dioxan	98	–
11	Dioxansulfur trioxide	Sodium phenolate	Dichloroethane + + dioxan	90-92	–

* Taking into account the "bis-derivative" formed.

As can be seen from the data in the table (exp. 2-5) the introduction of one nitro group into the para-position in benzyl bromide somewhat decreased or, in any case, did not increase the relative yield of C-derivative of β-naphthol.**

** When sodium or lithium β-naphtholates were treated with p-nitrobenzyl bromide in a solution of boiling dioxan, besides O- and C-derivatives, other materials were also formed but these were not investigated closely. p-Methylsulfonylbenzyl bromide reacted similarly with Na-β-naphtholate. Extensive tar formation occurred when 2,4-dinitrobenzyl chloride or iodide reacted with Na-β-naphtholate.

p-Methoxybenzyl bromide (table, exp. 1) showed a much greater tendency for C-substitution. However, it has not been clarified whether in this case the C-p-methoxybenzylnaphthol-2 (I) was a primary substitution product or was formed as a result of O-p-methoxybenzylnaphthol-2 (II) isomerization. Actually, according to our observations, ether (II) may be converted into substance (I) in the presence of p-methoxybenzyl chloride or hydrogen chloride.

In contrast to benzyl bromide [1], 4-bromo-1,3-dinitrobenzene (table, exp. 6) and benzoyl chloride reacted with Na-β-naphtholate in a boiling dioxan medium only at the oxygen atom. The substitution of a slightly polar solvent (toluene) for the dioxan did not change the direction of the benzoylation (table, exp. 7). At the same time, it is known that sodium phenolates and naphtholates are alkylated by such halogen derivatives as benzyl chloride or allyl bromide in slightly polar solvents (toluene, benzene), almost exclusively in the nucleus [2].

The higher tendency of acyl halides to give O-derivatives with metal phenolates was shown in the reaction between acetyl chloride and dichloroaluminum phenolate in a solution of boiling CS_2 (table, exp. 8). O-Acylation can hardly be explained by a specific effect of the solvent, as in the absence of solvent (without heating) [3] or in a boiling benzene medium [4] full aluminum phenolates were converted into esters by acyl chlorides; acylation at a higher temperature gave hydroxyketones (for example [3, 4]).

In contrast to triphenylmethyl chloride, tri-p-nitrophenylmethyl bromide, being a stronger electrophilic reagent, reacted with Na-phenolate exclusively at the O-atom, i.e., without transference of the reaction center (table, exp. 9, 10).

In comparison with the halogen derivatives, dioxansulfur trioxide is an extremely strong electrophilic reagent. It is capable of sulfonating (in a CCl_4 medium) not only anisole (in several minutes) and naphthalene, but also benzene [5]. When sodium phenolate was treated with dioxansulfur trioxide (table, exp. 11) the only reaction product was sodium phenyl sulfate.*

The main results of this work were explained after a thorough examination of the effects of various factors, including the reagent, on the direction of substitution in metal derivatives capable of reacting in two forms [7].

EXPERIMENTAL

Reaction of p-methoxybenzyl, benzyl and p-nitrobenzyl bromides with Na-β-naphtholate in acetone.

a) Reaction with p-methoxybenzyl bromide. The reaction was performed in an atmosphere of nitrogen. 9 ml of a solution of 3.32 g of Na-β-naphtholate in anhydrous acetone was added over a period of 45 minutes to 4.44 g of p-methoxybenzyl bromide (b.p. 107° at 5 mm) [8] in 4 ml of acetone at 56-57° (bath temperature). The mixture was heated for a further 30 minutes at 56-58° and then after cooling, shaken with dilute sulfuric acid and benzene. The organic layer was separated and the solvent evaporated. The residue was separated into neutral and acid fractions using an aqueous methanol solution of potassium hydroxide [1] (first without the use of an organic solvent and then in the presence of petroleum ether). The first fraction was recrystallized from a mixture of benzene and acetone. We obtained 2.5 g (47%) of substance (II), which was insoluble in aqueous and alcoholic alkali and had m.p. 151-151.5°.

Found %: C 82.11, 82.21; H 6.17, 6.09. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.10.

The acid fraction (2.34 g) was recrystallized twice from toluene to give 1.25 g of substance (I), which in all probability was 1-p-methoxybenzylnaphthol-2 with m.p. 130-131°. Substance (I) was soluble in dilute aqueous sodium hydroxide solution.

Found %: C 82.12, 82.28; H 6.32. 6.25. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.10.

b) Reaction with benzyl bromide. The experiment was performed as above. For the reaction we used 3.76 g of benzyl bromide (in 4 ml of acetone) and 9 ml of Na-β-naphtholate solution. One recrystallization of the neutral fraction (4.48 g) from alcohol yielded 3.85 g (82%) of the benzyl ether of β-naphthol with m.p. 98-99°. The melting point of the pure substance was 101-102°. A mixed melting point with an authentic preparation [1] (m.p. 101-102°) was not depressed. After precipitation of β-naphthol with mercury acetate [1], the acid fraction yielded 0.06 g of impure 1-benzylnaphthol-2.

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*Phenol also gave phenylsulfuric acid with pyridinesulfur trioxide [6] at 50° and dioxansulfur trioxide [5].

c) Reaction with p-nitrobenzyl bromide. For the reaction we used 4.76 g of p-nitrobenzyl bromide (in 4 ml of acetone) and 9 ml of Na-β-naphtholate solution. The experiment was performed similarly to the previous one with the exception that a 10% aqueous solution of sodium hydroxide was used instead of the alkali in aqueous methanol. We isolated neutral (5.72 g) and acid (0.26 g) fractions. Recrystallization of the neutral fraction from alcohol yielded 4.86 g (87%) of the p-nitrobenzyl ether of β-naphthol with m.p. 109-111°; the pure substance melted at 112.5-113° (from a mixture of alcohol and acetone); it did not depress the melting point of an authentic sample (prepared from Na-β-naphtholate and p-nitrobenzyl chloride in alcohol) [9], m.p. 111.5-112.2° (according to literature data [9] 106.7°). After removal of the β-naphthol, the acid fraction yielded 0.06 g of red-brown crystals, which were apparently impure 1-p-nitrobenzylnaphthol-2.

Reaction of benzyl and p-nitrobenzyl bromides with Na-β-naphtholate in benzene–acetone solution. a) Reaction with p-nitrobenzyl bromide. 9 g of Na-β-naphtholate was dissolved in a mixture of anhydrous benzene and acetone (10 ml of each). 12.5 ml of this solution of naphtholate was added over a period of 2 hours to a solution of 4.42 g of p-nitrobenzyl bromide in 4 ml of acetone and 4 ml of benzene at 55-57° (bath temperature). After 1 hour (same temperature), the reaction mixture was mixed with 0.1 N hydrochloric acid solution and extracted with benzene. The benzene layer was separated and the solvent evaporated. The residue was treated with aqueous methanolic alkali and then subsequently with 10, 5 and 2.5% aqueous sodium hydroxide to give neutral (5.1 g) and acid (0.34 g) fractions. The first was recrystallized from alcohol to give 4.59 g (85%) of the p-nitrobenzyl ether of β-naphthol with m.p. 107-110°; recrystallization from a mixture of methanol and acetone raised the m.p. to 112.5-113°. After removal of the β-naphthol (precipitation of 0.26 g of 1-acetomercurinaphthol-2), the acid fraction yielded 0.2 g of a solid brown mass.

b) Reaction with benzyl bromide. The reaction was performed as above with 3.5 g of benzyl bromide. The residue from evaporation of the benzene was treated with alkali in aqueous methanol. Crystallization of the neutral fraction from alcohol (3.4 g of substance with m.p. 91-94°) and then from methanol gave 2.44 g (54%) of the benzyl ether of β-naphthol with m.p. 101-101.5°. After removal of the naphthol (precipitation of 0.84 g of 1-acetomercurinaphthol-2) and recrystallization from formic acid, the acid fraction yielded 0.14 g (3%) of 1-benzylnaphthol-2 with m.p. 108-111°; the pure substance melted at 111-112°; it did not depress the melting point of an authentic sample [1].

Reaction of p-nitrobenzyl bromide with Li-β-naphtholate. 10 ml of a solution of Li-β-naphtholate in dioxan was added to 2.5 g of p-nitrobenzyl bromide in 10 ml of dioxan * over a period of 2 hours at 103-105° (bath temperature). The mixture was heated for a further 2 hours at 105-116°. As before, acid and neutral fractions were isolated using alkali in aqueous methanol. After precipitation of the β-naphthol with mercury acetate, the first of the fractions yielded 0.4 g (14%) of what in all probability was 1-p-nitrobenzylnaphthol-2 with m.p. 131-132° (from a mixture of benzene and petroleum ether).

Found %: N 4.95, 4.92. $C_{17}H_{13}O_3N$. Calculated %: N 5.01.

The substance formed golden yellow needles, which were readily soluble in dilute solutions of sodium hydroxide. A red salt was formed with strong solutions of the alkali.

Boiling the neutral fraction with alcohol (60 ml) extracted 0.6 g (20%) of the p-nitrobenzyl ether of β-naphthol. Fractional crystallization of the residue from acetone gave two substances with m.p. 242-244° (possibly 4,4'-dinitrostilbene) and 155-157°, which were not examined thoroughly.

Reaction of 4-bromo-1,3-dinitrobenzene with Na-β-naphtholate. The reaction was performed in an atmosphere of nitrogen. A solution of naphtholate, prepared from 0.80 g of β-naphthol and 0.12 g of sodium in 5 ml of dioxan was added over a period of 1 hour to a solution of 1.24 g of 4-bromo-1,3-dinitrobenzene in 5 ml of dioxan at 104-106° (bath temperature). The reaction mixture was heated at the same temperature for a further 0.5 hours; it was then cooled, mixed with 0.1 N hydrochloric acid solution and extracted with ether. The residue left after evaporation of the ether was treated several times with 10% KOH solution. The solid 2,4-dinitrophenyl ether of β-naphthol was washed with water, dried (1.6 g) and treated with ether. We obtained 1.4 g (67%) of the ether with m.p. 92-93°. After recrystallization from benzene, the substance had m.p. 93-94° (according to literature data [10], 95°). Acidification of the alkaline solution and extraction with ether gave 0.1 g of tar.

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* With the reverse addition order, considerable tar formation was always observed (especially with Na-β-naphtholate).

Reaction of benzoyl chloride with Na-β-naphtholate. 1.5 g of benzoyl chloride was added to a suspension of Na-β-naphtholate in 15 ml of toluene (the naphtholate was prepared by boiling a toluene solution of 1.6 g of β-naphthol and 0.23 g of sodium and then filtering in a stream of nitrogen), heated on a boiling water bath. The mixture was heated for 1 more hour, diluted with benzene and extracted several times with 10% aqueous sodium hydroxide solution. The alkaline extract was made acid to congo with hydrochloric acid. The organic materials were extracted with ether. The residue from evaporation of the ether was a trace of a red-brown oil. The solvent was evaporated from the neutral solution. We obtained 2.23 g (90%) of β-naphthyl benzoate. It was treated with small portions of ether and then had m.p. 105-106° (according to literature data: [11] 107°, [12] 106°). Benzoylation of Na-β-naphtholate in boiling dioxan in exactly the same way gave only β-naphthyl benzoate.

Reaction of acetyl chloride with dichloroaluminum phenolate. To prepare the dichloroaluminum phenolate [13], a solution of 6.75 g of phenol in 30 ml of CS_2 was added to 9 g of sublimed $AlCl_3$ in 60 ml of CS_2 (vigorous evolution of hydrogen chloride). 5.3 g of acetyl chloride was added in several portions to the solution of phenolate obtained, heated almost to boiling. The solution boiled up. The following day the mixture was decomposed with water. The carbon disulfide layer was separated from the aqueous one and the latter extracted with CCl_4. The combined organic solutions were washed with 10% sodium hydroxide solution (twice with 50 ml each time) and dried. Distillation yielded 8 g (87%) of phenyl acetate with b.p. 190-196°. On redistillation, the substance boiled over the range 192-194° (7 g obtained), while the bulk came over at 194° (according to literature data [14], b.p. 195.7°). The alkaline extract yielded 0.4 g of a liquid (possibly o-acetylphenol).

Reaction of triphenylmethyl chloride with Na-phenolate. A solution of 1.0 g of phenolate in 5 ml of dioxan was added to a solution of 1.40 g of triphenylmethyl chloride in 10 ml of dioxan at 103-105° (bath temperature) over a period of 0.5 hours. The reaction mixture was heated at the same temperature for a further 0.5 hours and treated as described previously [1]. We obtained 0.13 g (8%) of p-hydroxytetraphenylmethane with m.p. 280-282°, 0.55 g (38%) of the triphenylmethyl ether of p-hydroxytetraphenylmethane (bis derivative) with m.p. 201-203° and 0.38 g (22%) of the phenyl ether of triphenylcarbinol* with m.p. 101-102° and 0.3 g of a mixture of the two latter substances.

Reaction of tri-p-nitrophenylmethyl bromide with Na-phenolate. We used 2.3 g of tri-p-nitrophenylmethyl bromide [15] and 1.0 g of Na-phenolate. The reaction was performed exactly as the previous one. A preliminary experiment established that under the given conditions the reaction went to completion and that the phenyl ether of tri-p-nitrophenylcarbinol (III), precipitated in the presence of dioxan, contained dioxan of crystallization. The still hot reaction mixture was diluted with 20 ml of boiling water. The crystals which deposited on cooling were filtered off and dried in a vacuum desiccator over P_2O_5. We obtained 2.45 g of the ether (III) with m.p. 199-200° (decomp.). A solution of 1 g of this product in hot dioxan (about 7 ml) was poured into 25 ml of aqueous methanolic alkali with stirring. After cooling the precipitate was filtered off and washed with alkali and water. It was dried in a vacuum desiccator over solid NaOH. We obtained 1.13 g of (III) (containing dioxan) with m.p. 203-205° (with decomp.). The yield was 98% (allowing for a molecule of dioxan of crystallization). Acidification of the alkaline solution, extraction with ether and benzene and evaporation of the solvents yielded traces of tarry substances. For purification, ether (III) was recrystallized from dioxan and had m.p. 206° (decomp.).

Found %: C 62.35, 62.20; H 4.92, 4.90. $C_{25}H_{17}O_7N_3 \cdot C_4H_8O_2$. Calculated %: C 62.25; H 4.61.

The substance was insoluble in dilute alkalis and a saturated alcohol solution of sodium alcoholate. Gaseous hydrogen was not evolved when (III) was heated with metallic sodium in toluene or dioxan.

To prepare the ether without dioxan of crystallization, 0.6 g of the substance was dissolved in 250 ml of boiling ligroin (120°). Part of the ligroin (about 50 ml) was distilled off. The solution was filtered hot. On cooling it deposited fine, colorless needles. The m.p. was 205.5° (decomp.).

Found %: C 63.91, 63.79; H 3.84, 3.77. $C_{25}H_{17}O_7N_3$. Calculated %: C 63.70; H 3.65.

Hydrolysis of ether (III). A mixture of 0.32 g of ether (III), containing dioxan, 15 ml of alcohol and 1 g of NaOH was heated for several days, then acidified and then phenol extracted from the filtrate with ether and determined as tribromophenol after the usual operations; the yield was 0.17 g (92%) and the m.p. 91-93°. A mixed melting point with an authentic preparation (m.p. 92.5-93.3°) was not depressed. Ether (III) was readily hydrolyzed when heated for 15 minutes in glacial acetic acid in the presence of concentrated hydrochloric acid and stannous chloride.

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* The phenyl ether of triphenylcarbinol is unchanged under the reaction conditions and therefore it does not isomerize to the C-substituted phenol.

Reaction of dioxansulfur trioxide with Na-phenolate. The reaction was performed with the careful exclusion of moisture. The dioxansulfur trioxide [16] was prepared from 3.72 g of sulfur trioxide, 10 ml of dioxan and 20 ml of dichloroethane. The dioxansulfur trioxide dissolved almost completely. Part of this mixture, containing 3.23 g of SO_3, was used for the reaction. With shaking, the dioxansulfur trioxide was added portionwise to a solution of Na-phenolate, prepared by boiling (5 hours) a mixture of 25 ml of dioxan, 5.0 g of phenol and 1.6 g of sodium (the excess sodium was separated by filtration). A white precipitate of sodium phenyl sulfate was rapidly formed. After 3 hours, the reaction mixture (a test for sulfur trioxide with aqueous $BaCl_2$ solution was negative) was mixed with a dilute solution of NaOH and shaken with ether. The aqueous layer was separated, washed with ether and diluted to 250 ml with water. The sulfate ion content of 50 ml of this solution was determined. We obtained 0.02 g of $BaSO_4$, which corresponds to 1.1% of the SO_3 added to the reaction.

The amount of bound phenol was determined quantitatively in another portion (50 ml) of the solution. The cooled solution was made acid to congo with dilute hydrochloric acid. The mixture was extracted several times with ether to remove free phenol. 5 ml of concentrated hydrochloric acid was added to the aqueous solution, which was boiled for 5 minutes and then quickly cooled. The phenol liberated was extracted with ether. The aqueous solution did not decolorize bromine water, indicating that substituted phenol was absent. The phenol was extracted from the ether extract with alkali and precipitated with bromine water in an acid medium. The tribromophenol obtained (2.23 g) was purified by recrystallization from aqueous methanol to give 2.09 g (80%) with m.p. 91-92°.

The amount of sodium phenyl sulfate in 50 ml of the solution was determined quantitatively as the bound sulfuric acid. After the addition of excess barium chloride, the solution was filtered, made weakly acid and mixed with 5 ml of concentrated hydrochloric acid (no precipitate formed in the cold). The mixture was boiled for 5 minutes. We obtained 1.73 g (90%) of $BaSO_4$. The water was removed from another 50 ml portion of the sodium phenyl sulfate solution in vacuum. The crystalline residue was treated with anhydrous alcohol. The alcohol solution was filtered free from undissolved precipitate (it contained sulfate ion) and evaporated in vacuum until crystallization began. The addition of a small amount of ether precipitated colorless, scaly crystals. They were filtered off, washed with alcohol and dried in vacuum desiccator over P_2O_5. We obtained 0.7 g (44%) of sodium phenyl sulfate. The salt was extremely soluble in water, readily soluble in alcohol and hygroscopic [17]. It was hydrolyzed by dilute hydrochloric acid slowly in the cold and rapidly on heating to give phenol and sulfate ion.

0.287 g of the salt in acid $BaCl_2$ solution was boiled for 20 minutes to give 0.327 (95.7%) of $BaSO_4$. Under similar conditions, but in the absence of $BaCl_2$, 0.20 g of the salt was hydrolyzed. We obtained 0.31 g (94.7%) of tribromophenol with m.p. 88-90°. Recrystallization raised the m.p. to 92.5-93.5°.

The dioxansulfur trioxide prepared from 4.2 g of SO_3 in 10 ml of dioxan and 20 ml of dichloroethane, was added in one portion to a solution of phenolate, prepared as previously, starting from 5 g of phenol and 20 ml of dioxan. Heat was evolved. After 3 hours, the precipitate was filtered off, washed twice with absolute ether and dried in a vacuum desiccator over P_2O_5. We obtained 9.47 g (92%) of sodium phenyl sulfate.

Preparation of p-methylsulfonylbenzyl bromide (IV). From a dropping funnel, with an end reaching to the bottom of the flask, 20 g of bromine was added over a period of 10 minutes to 17 g of methyl-p-tolylsulfone at 170-190° (bath temperature); the mixture was heated for 1 hour and dissolved in 50 ml of hot benzene (decolorized with charcoal). On cooling the solution deposited colorless needles of (IV) with m.p. 95-95.8°.

Found %: C 38.70, 38.60; H 3.87, 3.91. $C_8H_9O_2BrS$. Calculated %: C 38.57; H 3.64.

With $AgNO_3$ in alcohol, substance (IV) rapidly gave a precipitate of AgBr and the bromine was quite readily eliminated by heating with alkalis. Reaction with sodium iodide in acetone gave an iodide with m.p. 119-120° (from alcohol). On heating 0.75 g of (IV) with Na-β-naphtholate (from 1 g of β-naphthol and 0.08 g of sodium) in 17 ml of anhydrous alcohol, we obtained 0.5 g (50%) of the p-methylsulfonylbenzyl ether of β-naphthol (V) with m.p. 159-159.5° (from benzene).

Found %: C 69.51, 69.71; H 5.25, 5.35; S 10.05, 10.28. $C_{18}H_{16}O_3S$. Calculated %: C 69.22; H 5.16; S 10.27.

As a result of reacting bromide (IV) with Na-β-naphtholate in boiling dioxan, we obtained ether (V) together with other neutral substances, which were not investigated more closely, and also a reaction product, which was soluble in alkalis and had m.p. 195-197° (from a mixture of benzene and methanol).

SUMMARY

We studied the effect of the reagent's character on the relative yields of O- and C-derivatives, using as examples some alkylation and acylation reactions of phenolates and β-naphtholates.

Received January 28, 1957

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* Original Russian pagination. See C. B. Translation.

SOME ESTERS OF γ-CHLOROCROTYL ALCOHOL

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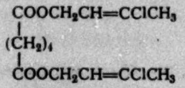
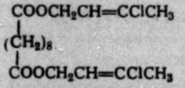
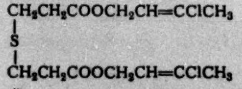
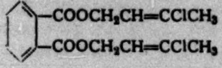
γ-Chlorocrotyl alcohol, obtained by the saponification of 1,3-dichlorobutene-2 [1], is a readily available substance. While the ethers of γ-chlorocrotyl alcohol are well known [1-3], its esters have not been studied (with the exception of the acetate [2]).

With the object of investigating the effect of the γ-crotyl group on some properties of esters we have synthesized a few representatives of this class of compound that have not been described previously. By reacting γ-crotyl alcohol with adipic, sebacic and thiodipropionic acids, and with phthalic anhydride[*] in the presence of p-toluenesulfonic acid, the corresponding esters were obtained (Table 1).

TABLE 1

γ-Chlorocrotyl Esters of Dibasic Acids

Formula	d_4^{20}	n_D^{20}	Yield (%)
 $\mathrm{COOCH_2CH{=}CClCH_3}$ $\mathrm{(CH_2)_4}$ $\mathrm{COOCH_2CH{=}CClCH_3}$	1.1674	1.4818	82
 $\mathrm{COOCH_2CH{=}CClCH_3}$ $\mathrm{(CH_2)_8}$ $\mathrm{COOCH_2CH{=}CClCH_3}$	1.1018	1.4778	80
 $\mathrm{CH_2CH_2COOCH_2CH{=}CClCH_3}$ S $\mathrm{CH_2CH_2COOCH_2CH{=}CClCH_3}$	1.1650	1.5095	78
	1.2412	1.5380	50

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[*] The preparation of the phthalate ester proceeded much more slowly and required a greater amount of catalyst than in the case of the other esters, and the reaction gave low yields. It seems to us that the low yields of di-γ-chlorocrotyl phthalate (the experiment was repeated with similar results) can be explained by the electronegative nature of the γ-chlorocrotyl group. As a consequence of this, the ester molecules, in which the ester groups occur close together in the alpha-position, form with difficulty. Indirect confirmation of this supposition is given by our unsuccessful attempt to prepare tri-γ-chlorocrotyl phosphate by the interaction of phosphorus oxychloride, γ-chlorocrotyl alcohol, and pyridine. On vacuum distillation, breakdown of the reaction product occurred.

In spite of the presence of two double bonds in the molecule of each of these esters and of rather high boiling points of the esters, the latter were distilled in vacuo, almost to dryness, without polymerizing. This appears to be the natural consequence of a powerful screening of the double bonds in the esters [4].

Comparative data on the boiling points, flash points, and specific resistivities of the esters obtained are given in Table 2, together with those of the known n-butyl esters of the same dibasic acids which are nearest to them (in length of carbon chain).

TABLE 2

Some Properties of γ-Chlorocrotyl and n-Butyl Esters of Dibasic Acids

Substance	Boiling point (pressure in mm)	Flash point	Specific resistivity (in Ω/cm)
Di-γ-chlorocrotyl adipate	160-162° (2.5), 188-189 (4)	193°	$1 \cdot 10^8$
Dibutyl adipate	143 (2-2.5)	157	$2 \cdot 10^{10}$
Di-γ-chlorocrotyl sebacate	208-209 (2-2.5)	216-217	$1 \cdot 10^8$
Dibutyl sebacate	178-180 (1.5-2)	198	–
(Di-γ-chlorocrotyl)-thiodipropionate	200-202 (4)	213	$1 \cdot 10^8$
(Dibutyl)-thiodipropionate	170-171 (3.5-4)	175	$1.4 \cdot 10^{10}$
Di-γ-chlorocrotyl phthalate	189-191 (2-2.5)	201	Less than $1 \cdot 10^8$
Dibutyl phthalate	148 (1), 182 (5)	170	$3.6 \cdot 10^9$

From the data of Table 2 it is evident that substitution of butyl by γ-chlorocrotyl radicals in the dibasic esters brings about an increase in boiling point of 10-15° (at 2-2.5 mm), an increase in flash point of 10-20° and a marked decrease in the specific resistivity (of approximately the second order).

EXPERIMENTAL

γ-Chlorocrotyl alcohol [1]. By reacting 1560 g of 1,3-dichlorobutene-2 with a solution of 1480 g of sodium carbonate in 5.6 liters of water at 70-95° for 5 hours, 900 g (68%) of γ-chlorocrotyl alcohol was obtained.

B.p. 159-161°, 88-90° (50 mm), d^{20}_4 1.1053, $n^{20}D$ 1.4660. Literature data [1]: b.p. 92° (50 mm), d^{20}_{20} 1.106, $n^{20}D$ 1.4652.

γ-Chlorocrotyl adipate. In a three-necked flask fitted with a stirrer, thermometer and L-shaped outlet tube (the latter connected to a condenser and receiver), 100 g adipic acid, 218 g γ-chlorocrotyl alcohol and 2 g p-toluenesulfonic acid were mixed. The mixture was stirred at 95-110° and 70 mm residual pressure (for the more rapid removal of water formed). Esterification was continued for 7 hours (to an Acid Number of 5.6). The reaction mixture was neutralized with 2% alkali solution, washed with water, the water and excess alcohol were distilled off, and the residue was redistilled at 4 mm. The following fractions were taken: 1st fraction, b.p. 60-150°, 10 g; 2nd fraction, b.p. 150-188°, 2 g; 3rd fraction, b.p. 188-189°, 182 g – di-γ-chlorocrotyl adipate. The 3rd fraction was a yellow, clear liquid with an unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 21.93. Saponification coefficient 350; acid number 0.3. $C_{14}H_{20}O_4Cl_2$.
Calculated %: Cl 21.94. Saponification coefficient 346.5; acid number 0.0.

γ-Chlorocrotyl Sebacate. The reaction was carried out in the same way as above. By the reaction of 102 g sebacic acid and 160 g γ-chlorocrotyl alcohol in the presence of 3 g p-toluenesulfonic acid at 65-100° and 70-80 mm for 7 hours, 150 g (80%) of di-γ-chlorocrotyl sebacate was obtained. A yellow, clear liquid with an unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 18.7. Saponification coefficient 301, 302; acid number 0.26. $C_{18}H_{28}O_4Cl_2$.
Calculated %: Cl 18.69. Saponification coefficient 295.3; acid number 0.0.

γ-Chlorocrotyl thiodipropionate. By the reaction of 60 g thiodipropionic acid and 95 g γ-chlorocrotyl alcohol in the presence of 1 g toluenesulfonic acid at 65-105° and 60-80 mm for 5 hours, 93.5 g (78%) of (di-γ-crotyl)-thiodipropionate. A clear, yellow liquid with a faint, unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 19.8. Saponification coefficient 321; acid number 0.4. $C_{14}H_{20}O_4Cl_2S$.
Calculated %: Cl 19.96. Saponification coefficient 315; acid number 0.0.

γ-Chlorocrotyl Phthalate. By the reaction of 153 g phthalic anhydride and 328 g γ-chlorocrotyl alcohol in the presence of 7 g p-toluenesulfonic acid at 90-110° and 70-75 mm for 12 hours, 172 g (50%) of di-γ-chlorocrotyl phthalate was obtained. A clear, yellow-orange, odorless liquid, solidifying at 14-15° to light-yellow crystals, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 20.43. Saponification coefficient 319; acid number 0.3. $C_{16}H_{16}O_4Cl_2$. Calculated %: Cl 20.66. Saponification coefficient 326.3; acid number 0.0.

Determination of the flash points of the esters was carried out (by the Brenken method) in an open cup. The specific resistivity was measured according to GOST 6581-53.

SUMMARY

Some previously unknown esters of γ-chlorocrotyl alcohol and dibasic acids have been prepared and characterized.

Received January 24, 1957

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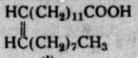
THE CONFIGURATIONAND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

VIII. THE REACTIVITY OF ERUCIC AND BRASSIDIC ACIDS AND THEIR ESTERS

A. K. Plisov and N. V. Bulatova

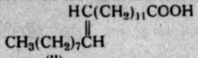
Examination of the properties of erucic and brassidic acids, and also of their esters, is of definite interest. The characteristic properties, connected with the spatial structure of the octadecenic acids and their esters were investigated sufficiently in a number of previous papers [1]. The necessity is therefore quite obvious for a similar systematic study of the reactions of erucic and brassidic acids and their esters, according to the position of the double bond, and also of reactions connected with the ester group. Hydrogenation, oxidation and saponification reactions are involved in this connection. On the basis of a study of these reactions the question of the configuration of erucic and brassidic acids, which up to the present time has not been established reliably by chemical means, can be clarified.

On the basis of determination of the cryoscopic constants, Mascarelli [2] attributed to erucic acid the cis-configuration (I), and to brassidic acid the trans-configuration (II).



$$\begin{matrix} HC(CH_2)_{11}COOH \\ \| \\ HC(CH_2)_7CH_3 \end{matrix}$$

(I)



$$\begin{matrix} \qquad\qquad HC(CH_2)_{11}COOH \\ \qquad\qquad \| \\ CH_3(CH_2)_7CH \end{matrix}$$

(II)

G. V. Pigulevskii and P. A. Artamonov [3], taking into account the difference in the frequencies of the Raman spectra due to the double bonds, also decided that erucic acid has the cis, and brassidic acid the trans-structure. Assuming that in the given case the spatial structure must show up in the chemical transformations of these acids we carried out the experiments described below. The results confirm the conclusion made on the basis of the physical methods, relegating erucic acid to the cis-series and brassidic acid to the trans-series. Erucic acid and its esters hydrogenate and oxidize more rapidly than brassidic acid and its esters, but erucates saponify more slowly than brassidates.

EXPERIMENTAL

Isolation of erucic acid from rapeseed oil. In distinction from the known methods of isolating erucic acid from fatty oils [4], we used the following method for its preparation from rapeseed oil, based on the good solubility of lead erucate in hot alcohol. To the mixture of fatty acids isolated from 200 g of rapeseed oil dissolved in 200 ml alcohol and heated on a water-bath, a boiling solution of 80 g of lead acetate in 100 ml alcohol was added. After boiling for a short time the solution was transferred to a well-heated separating funnel in which it was allowed to settle for 1-1.5 minutes. Then the liquid massof lead salts of saturated acids, insoluble in hot alcohol, were separated from the solution and washed 2-3 times with 50-75 ml of boiling alcohol for the removal of coprecipitated lead erucate. The alcohol washings were combined with the main portion and kept for 7-8 hours at 2-3°. The clear solution was then decanted from the separated lead erucate and the latter decomposed with dilute hydrochloric acid (1 : 5). The supernatant oily layer of crude erucic acid, formed by heating and salting out, was washed with hot water and recrystallized from a 3-4-fold volume of alcohol.

Brassidic acid was obtained by the action of oxides of nitrogen on erucic acid according to the method of Holde [5].

The methyl and butyl esters of erucic and brassidic acid were prepared by direct esterification of the acids (1 ml) by the corresponding alcohol (3 ml) in the presence of conc. H_2SO_4 (1% on the fatty acid). The butyl ester of brassidic acid, not described in the literature, was prepared by us for the first time.

Found: acid number 0; saponification number 142.4. $C_{26}H_{50}O_2$. Calculated: saponification number 142.17.

The physical constants of the substances investigated are quoted below (Table 1).

TABLE 1

	Erucic acid	Brassidic acid	Methyl erucate	Methyl brassidate	Butyl erucate	Butyl brassidate
Melting point	34°	61°	–	34-35°	–	33-35°
Boiling point	–	–	220-221° (at 5 mm)	224° (at 5 mm)	244° (at 7 mm)	246° (at 7 mm)
n_D	1.4473 (at 55°)	1.4460 (at 58°)	1.4558 (at 20°)	1.4490 (at 35°)	1.4555 (at 20°)	1.4549 (at 20°)

The erucic and brassidic acids and their methyl and butyl esters (1 mole) were oxidized with $K_2Cr_2O_7$ (1.5 moles) in glacial acetic acid at the same temperature in each case. The course of the reaction was followed by determination of the unreacted oxidizing agent by iodometric titration of the reaction mixture. A weighed sample of the substance (1/2000 mole, i.e., 0.1691 g of the acids, 0.1761 g of the methyl esters and 0.1977 g of the butyl esters) was dissolved in glacial acetic acid in a 10 ml measuring flask, the solution transferred to a flask with a ground-glass stopper and the measuring cylinder washed out with 3 ml of the solvent. [After the solution of isomer stood in a thermostat at 55 or 40° for half an hour and a solution of the oxidizing agent stood in a jacketed burette (also heated with water at 55 or 40°), 87 ml of the oxidizing agent solution was added to the solution of the substance to be oxidized.]. Immediately after mixing the solutions, the first determination of the oxidizing agent content in the reaction mixture was carried out (initial concentration).

The oxidation reaction rate constant was calculated from the equation

$$K = \frac{2.303}{t} \log \frac{\alpha}{\alpha - x},$$

where: α is the initial oxidizing agent concentration in percent (100%), and x is the quantity of oxidizing agent reacted after time t.

Data for the oxidation of erucic and brassidic acids and their esters are given in Table 2.

In order to examine the question of the course of the oxidation reaction 3.4 g of erucic and brassidic acids in glacial acetic acid was oxidized with $K_2Cr_2O_7$ (4.5 g) under the conditions described above. On completion of oxidation the reaction product was neutralized and evaporated to dryness. The residue was decomposed with dilute sulfuric acid and steam-distilled. Since about 1 g of pelargonic acid, identified by its melting point (12.5°) and refractive index ($n^{20}D$ 1.4306), was found in the steam distillates, it can be presumed that the oxidation of erucic and brassidic acids, under our chosen conditions, follows the same course, and is associated with scission of their molecules at the double bond.

Catalytic hydrogenation of erucic and brassidic acids, methyl erucate, methyl brassidate, butyl erucate and butyl brassidate was carried out simultaneously in hydrogenation flasks at 23°. Mechanical agitation was performed by means of a magnetic stirrer. Pd on $BaSO_4$ from the same preparation was used as catalyst; the solvent was ethyl acetate. 1/2000 mole of isomer in 5 ml ethyl acetate was added to the catalyst, saturated with hydrogen (0.02 g Pd/$BaSO_4$ or 0.0005 g Pd) in 3 ml ethyl acetate in a stream of hydrogen. The results of hydrogenation are given in Table 3.

The hydrogenation reaction rate constants are calculated from the equation

$$K = \frac{2.303}{t} \log \frac{\alpha}{\alpha - x},$$

where; α is the quantity of hydrogen required for complete saturation of the sample in percent; $\alpha - x$ is the quantity of hydrogen combined with the sample after time t, in percent.

TABLE 2

Oxidation of Erucic and Brassidic Acid and Their Esters with $K_2Cr_2O_7$ in Acetic Acid at 55 and 40°.

t (in hours)	Erucic acid		Brassidic acid		Methyl erucate		Methyl brassidate		Butyl erucate		Butyl brassidate	
	x	K	x	K	x	K	x	K	x	K	x	K
15	43.9	0.039	28.3	0.022	29.2	0.023	18.4	0.014	28.1	0.022	17.8	0.013
21	53.2	0.036	34.7	0.020	39.6	0.024	26.0	0.014	34.7	0.020	21.6	0.012
30	63.0	0.033	41.2	0.018	45.0	0.020	31.4	0.013	43.4	0.019	27.1	0.011
64	83.0	0.036	65.7	0.018	71.1	0.020	52.1	0.012	67.3	0.019	45.0	0.010
80	95.1	0.038	73.8	0.017	80.4	0.020	61.9	0.012	76.6	0.019	53.2	0.010
108	100	—	85.8	0.018	91.3	0.022	77.1	0.014	86.9	0.019	67.3	0.010
136	—	—	92.3	0.019	100	—	91.2	0.017	92.8	0.019	79.8	0.011
	$K_{av}^{55°}=0.036$ $K_{av}^{40°}=0.019$		$K_{av}^{55°}=0.018$ $K_{av}^{40°}=0.011$		$K_{av}^{55°}=0.021$ $K_{av}^{40°}=0.012$		$K_{av}^{55°}=0.013$ $K_{av}^{40°}=0.008$		$K_{av}^{55°}=0.019$ $K_{av}^{40°}=0.0094$		$K_{av}^{55°}=0.011$ $K_{av}^{40°}=0.007$	
Activation energy	8363		8183		8297		7660		8986		7386	
Probability constant	$1.1 \cdot 10^8$		$8.56 \cdot 10^7$		$1.01 \cdot 10^8$		$3.85 \cdot 10^7$		$2.91 \cdot 10^8$		$2.54 \cdot 10^7$	

TABLE 3

Hydrogenation of Erucic and Brassidic Acids and their Esters in the Presence of Pd at 23°

t (in min)	Erucic acid		Brassidic acid		Methyl erucate		Methyl brassidate		Butyl erucate		Butyl brassidate	
	$\alpha - x$	K	$\alpha - x$	K	$\alpha - x$	K	$\alpha - x$	K	$\alpha - x$	K	$\alpha - x$	K
60	8.26	0.0014	5.7	0.0010	6.6	0.0011	3.3	0.0006	3.3	0.0006	—	—
120	16.5	0.0015	9.9	0.0008	13.2	0.0012	7.3	0.0006	9.0	0.0008	4.9	0.0004
450	44.6	0.0012	33.8	0.0008	34.7	0.0009	24.7	0.0006	33.8	0.0009	19.8	0.0005
810	66.1	0.0014	57.7	0.0010	56.2	0.0011	44.6	0.0007	52.8	0.0009	32.2	0.0005
1550	95.0	0.0019	87.6	0.0010	91.7	0.0016	72.7	0.0008	90.9	0.0015	56.2	0.0005
1800	100	—	91.7	0.0013	—	—	81.7	0.0009	—	—	61.9	0.0006
	$K_{av}=0.0014$		$K_{av}=0.0009$		$K_{av}=0.0011$		$K_{av}=0.0007$		$K_{av}=0.0009$		$K_{av}=0.0005$	

The hydrogenation of erucic and brassidic acids has already been described in the literature [6]. However, repetition of this was necessary for solution of the problem of the effect of the alcohol radical on the rate of hydrogenation. Moreover, the figures obtained by Paal [6], characterizing the rate of hydrogenation of oleic and elaidic acids seem to us to be somewhat approximate. In Paal's paper it is stated that oleic acid, for example, after 60 minutes absorbs about half as much hydrogen as erucic acid. This does not agree with the hydrogenation experiments on oleic and erucic acids repeated by Fokin [7]. The data obtained by one of us [1] on the hydrogenation of oleic acid and its esters confirms that erucic acid and its esters hydrogenate more slowly than oleic acid and its esters. The same applies to elaidic and brassidic acids and their esters.

Reduction of erucic and brassidic acids with hydriodic acid. For clarification of the results of the combination of hydrogen with erucic and brassidic acids in the absence of a catalyst, experiments were carried out on their reduction with a solution of HI. The experiments consisted in heating equal weights of the acids (6 g) to 110-115°, with HI solution, in high-melting sealed tubes for 30 hours (intermittent). After it separated from the reaction mixture, the reduction product was dissolved in a small quantity of petroleum ether and the bromine number was determined [8]. It was found that 95% of the erucic acid and 99% of the brassidic acid remained unchanged. When the erucic acid reduction product was treated with cold alcohol at 5° the erucic acid went into solution, and the residue after recrystallization from petroleum ether corresponded in acid number and melting point (82°) to behenic acid. The crude product from the reduction of erucic acid can be elaidinized. This reaction is not given by the brassidic acid reduction product. Hence under the conditions of uncatalyzed reduction of erucic and brassidic acids isomerization does not take place and the reduction of erucic acid in this case also is more rapid than that of brassidic acid.

Saponification of the methyl and butyl esters of erucic and brassidic acids was carried out under conditions described previously [9], in small beakers with lids containing sealed-in platinum electrodes. The course of saponification was followed by the change in electrical conductivity of the reaction mixture, the fall in which corresponded to the decrease in concentration of hydroxyl ions expended on saponification of the esters. The commencement of the reaction was taken as the moment of addition of the alcoholic KOH solution to the alcoholic solution of the isomer. The electrical conductivity was calculated from the resistance measured with an SK ohmmeter with an indicator lamp. Equal weights of the esters (1/1000 mole or 0.3522 g for the methyl and 0.3946 g for the butyl esters) were dissolved in 9 ml of 96% alcohol and kept in a thermostat for half an hour at 25°. 1 ml of 1N alcoholic KOH was then added to the ester solution and the first determination of alkali content carried out immediately.

TABLE 4

Saponification of the Methyl and Butyl Esters of Erucic and Brassidic Acids at 25°

t (in hours)	Methyl erucate			Methyl brassidate			Butyl erucate			Butyl brassidate		
	Electrical conductivity	x	K	Electrical conductivity	x	K	Electrical conductivity	x	K	Electrical conductivity	x	K
0	303	—	—	303	—	—	303	—	—	303	—	—
5	278	8.1	0.00017	232	20.0	0.0005	283	6.7	0.0001	240	20.6	0.0005
17	244	19.5	0.00014	177	41.6	0.0004	255	15.9	0.0001	195	36.6	0.0003
21	229	24.4	0.00013	154	49.3	0.0005	241	19.3	0.0001	185	38.9	0.0003
30	213	29.5	0.00014	148	51.3	0.0004	236	22.2	0.0001	172	43.2	0.0003
44	159	35.3	0.00015	134	55.9	0.0003	221	26.4	0.0001	170	43.6	0.0002
	$K_{av} = 0.00015$			$K_{av} = 0.0001$			$K_{av} = 0.0001$			$K_{av} = 0.0003$		

The saponification reaction rate was calculated from the equation for a 2nd-order reaction

$$K = \frac{1}{t}\,\frac{x}{\alpha(\alpha - x)},$$

where: α is the initial electrical conductivity in percent (100%), x is the decrease in electrical conductivity after time t.

Results of experiments on the saponification of the methyl and butyl esters of erucic and brassidic acids are given in Table 4.

SUMMARY

1. A method for the isolation of erucic acid from rapeseed oil is proposed.

2. The butyl ester of brassidic acid, not described in the literature, has been prepared.

3. It is shown that erucic acid and its esters oxidize and hydrogenate more rapidly than the corresponding brassidic acid and its esters.

4. It is shown that the saponification of erucates proceeds more slowly than that of brassidates.

5. The oxidation, hydrogenation and saponification reactions of erucic and brassidic acids and their esters, in conformity with the spatial configurations, confirm the cis-structure of erucic acid and the trans-structure of brassidic acid.

Received January 19, 1957

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*Original Russian pagination. See C. B. Translation.

**In Russian.

THE CONFIGURATION AND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

IX. THE PROPERTIES OF THE α-METHYLCROTONIC ACIDS AND THEIR ESTERS

A. K. Plisov and N. P. Paladienko

In a previous communication [1], one of us has already shown that the α-methyl crotonic acids (angelic and tiglic), and also their esters, do not display the same reactivity. This was established by the example of the oxidation and saponification reactions. In these cases it was shown that angelic acids and its esters, as in all cases with other unsaturated acids described previously, oxidize at the double bond considerably more rapidly than tiglic acid and its esters, whereas saponification of the esters, on the other hand, proceeds more slowly with the former than with the latter. However Crűrős [2] in the hydrogenation of angelic and tiglic acids found conditions under which the former acid (cis-form) hydrogenates more slowly than the latter (trans-form). However, the quantity of catalyst used in these experiments exceeded that normally used, being some hundreds of times greater than the latter.

These circumstances served as a basis on which to widen our investigation of the α-methylcrotonic acids and to examine, in particular, their behavior on hydrogenation. This reaction has been described in considerable detail by one of us [3] in the case of crotonic acid and its esters, and obtaining such data for the α-methylcrotonic acids and their esters, in addition to clarifying other problems, should make it possible to decide the effect of the methyl group on this reaction. The presence of this group, in our opinion, must to some extent affect the rate of addition of hydrogen to the double bond.

The realization of such observations seems the more essential in that the α-methylcrotonic acids are analogous, in a number of their chemical reactions, to the crotonic acids, the configuration of which has been established by the method of combination dispersion of light.

With regard to differences in the reactivity of the cis- and trans-forms in the given case, this is explained by the fact that the space near the double-bond of the trans-form is occupied on both sides by groups of atoms, the volume of which is considerably greater than that of the hydrogen atom, and for the cis-form this space is less occupied on one side. It must be pointed out that the carboxyl group occupies the space near the double bond to a greater extent (its volume calculated by Kopp's formula is 36.5 cm^3/mole) than does the methyl radical (volume 27.6 cm^3/ mole). Steric hindrance, created by substitution at the double bond can be illustrated also by planar projections of the cis- (I) and trans-(II)-methylcrotonic acids (Fig. 1). The planar projections were constructed in conformity with the additivity rule, with conservation of the proportionality of the atomic radii, valence angles and length of bonds between the atoms.

We prepared the stereo-isomeric α-methylcrotonic acids and their ethyl, butyl, isobutyl and benzyl esters. The acids and esters were hydrogenated. The data so obtained are in full agreement with those of our previous papers [1]. The graphs (Figs. 2-4) show the course of hydrogen absorption by the acids and esters at two temperatures. Attention is attracted in the first place, to the fact that hydrogenation of the α-methylcrotonic acids proceeds more slowly than that of crotonic acid. In other words, the methyl group in the α-position to the carboxyl, evidently hinders addition of hydrogen to the double bond.

The results of these experiments fully coincide with the conclusions drawn previously in relation to the hydrogenation of the cis- and trans-forms of unsaturated acids and their esters [3]. The cis-forms hydrogenate more easily than the trans-forms. Furthermore, all the esters of the α-methylcrotonic acids hydrogenate with more difficulty than the acids themselves.

On comparing the hydrogenation rates it was noted that the free acids hydrogenate with the greatest difference in rates and their esters with the least difference. It is also of interest that the differences in hydrogenation rates show up to a greater extent on comparing the results of hydrogenation of the various esters of tiglic acid with one another and to a lesser extent in the case of the esters of angelic acid.

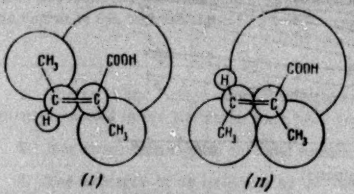

Fig. 1. Planar projection of α-methylcrotonic acid. I) Cis-acid; II) trans-acid.

From examination of the graphs, the effect of the size of the alcohol radical on the hydrogenation rate is also notable: the greater the volume of the alcohol radical, the slower the rate of hydrogenation of the ester.

Hydrogenation of the stereoisomeric α-methylcrotonic acids and their esters proceeds in an analogous manner with both palladium and platinum catalysts. A temperature reduction of 10° markedly reduces the rate of hydrogen addition.

In order to examine the nature of the addition of hydrogen to the α-methylcrotonic acids, experiments on the reduction of angelic and tiglic acids with hydriodic acid solution were carried out. In these uncatalyzed reduction experiments, the phenomena connected with adsorption on a metal are eliminated, and the results indicate an inherent difference in the aptitudes of the α-methylcrotonic acids with respect to the rate of hydrogen addition, as was established by the experiments, described above, on catalytic hydrogenation.

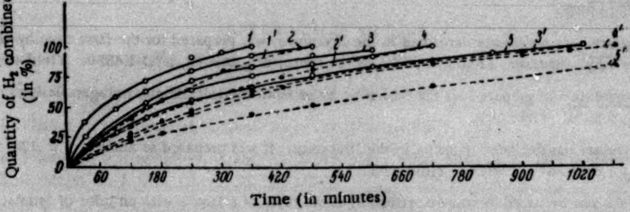

Fig. 2. Hydrogenation of angelic and tiglic acids and their esters on a Pd-catalyst at 25° in anhydrous ethanol. 1) Angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

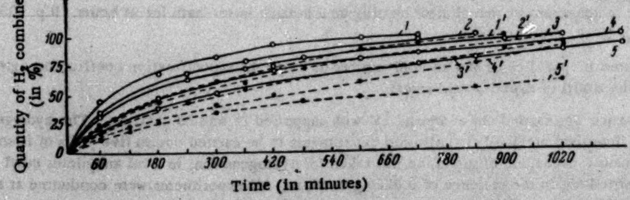

Fig. 3. Hydrogenation of angelic and tiglic acids and their esters on a Pd-catalyst at 15° in anhydrous ethanol. 1) angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

Thus the results of our experiments presented here, and also experiments described in other communications [4] confirm that angelic acid and its esters have the cis-configuration and tiglic acid and its esters correspond to the trans-configuration.

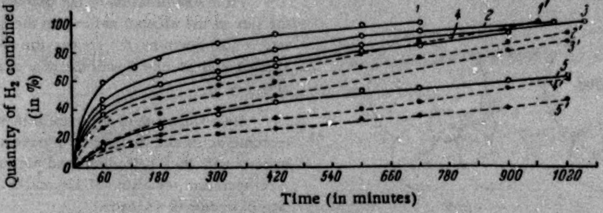

Fig. 4. Hydrogenation of angelic and tiglic acids and their esters on a Pt-catalyst at 25° in anhydrous ethanol. 1) Angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

EXPERIMENTAL

Angelic and tiglic acids were prepared as previously described by us [1].

Ethyl angelate was prepared from potassium angelate and ethyl iodide [5]. Liquid, b.p. 140-141°, $n^{24}D$ 1.4280, d^{12}_{12} 0.9276. Yield 38%.

Butyl angelate, not previously described in the literature, was prepared for the first time by us under the same conditions as for ethyl angelate. Liquid, b.p. 73-74° at 9 mm, d^{12}_{12} 0.9089, $n^{20}D$ 1.4350. Yield 40%.

Isobutyl angelate was prepared for the first time by us from the salt and the halogen derivative. B.p. 176-177°, $n^{20}D$ 1.448, d^{14}_{14} 0.8974. Yield 30%.

Benzyl angelate has not been reported in the literature. It was prepared as above. B.p. 125-126° at 6-7 mm, $n^{12}D$ 1.510, d^{12}_{12} 1.0366, d^{12}_{4} 1.0361. Yield 47%.

Ethyl tiglate was prepared by esterification [5] in the form of a liquid with an odor of fennel. B.p. 154°, $n^{12}D$ 1.440, $n^{15}D$ 1.4364, d^{12}_{4} 0.9349. Yield 78.1%.

Butyl tiglate has not been reported in the literature. We prepared it by esterification, as for ethyl tiglate. B.p. 189-191°, $n^{12}D$ 1.442, $n^{15}D$ 1.440, d^{12}_{12} 0.9141. Yield 72.5%.

Isobutyl tiglate has not been reported in the literature. We prepared it by esterification. B.p. 182-184°, $n^{12}D$ 1.439, $n^{15}D$ 1.437, d^{12}_{12} 0.9047. Yield 60%.

Benzyl tiglate has not been reported in the literature. It was obtained by us from potassium tiglate and benzyl chloride in anhydrous methanol after heating on a boiling water-bath for 24 hours. B.p. 139° at 9 mm, $n^{20}D$ 1.518, d^{12}_{12} 1.0431. Yield 56.5%.

All the esters prepared by us had an acid number of 0 and the saponification coefficients agreed with theory (within the limits of experimental error).

Hydrogenation was carried out at 25 and 15° with supported Pt and Pd catalysts. The hydrogenation apparatus, which has been described previously [3] allowed experiments to be carried out on five pairs of isomers simultaneously. In each experiment 0.0005 mole of substance was taken for hydrogenation, in 2 ml anhydrous ethyl alcohol. Hydrogenation was carried out in the presence of 0.0200 g catalyst. All experiments were conducted at atmospheric pressure, which fluctuated in different experiments between 768 and 754 mm.

Isolation and examination of the hydrogenation products consisted in removing the catalyst and solvent and subsequent application of the normal methods of purification of methylethylacetic acid and its esters. In all cases methylethylacetic acid and its ethyl, butyl and isobutyl esters, with constants in full agreement with the literature data, were isolated from the hydrogenation products.

Reduction of the α-methylcrotonic acids with hydriodic acid. Equal quantities of HI solution were placed in high-melting glass tubes and equal weights (0.3 g) of the α-methylcrotonic acids were added. The sealed tubes with their contents were heated at 110-115° for 24 hours. After opening the tubes and isolating the reaction products it was found (by titration with a solution of bromine in potassium bromide) that the angelic acid had reacted to the extent of 6%, and the tiglic to 1%

SUMMARY

1. The butyl and benzyl esters of angelic acid and the butyl, isobutyl and benzyl esters of tiglic acid, not previously reported in the literature, have been prepared for the first time.

2. It is shown that angelic acid and its esters hydrogenate more rapidly than tiglic acid and its esters.

3. The existence of an influence by the alcohol radical on the course of the hydrogenation reaction is established.

4. A difference is shown in the effect of the alcohol radical of the cis- and trans-esters on the hydrogenation reaction.

5. Differences in the relative rates of hydrogenation of the α-methylcrotonic acids and their esters confirm the classification of angelic acid and its esters in the cis-series and tiglic acid and its esters in the trans-series.

Received January 26, 1957

Odessa State University.

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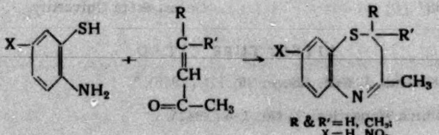
*Original Russian pagination. See C. B. Translation.

THE CONDENSATION OF o-AMINOTHIOPHENOLS WITH UNSATURATED KETONES AND β-HALOKETONES. II

L. K. Mushkalo

In the first communication it was shown [1] that on condensation of o-aminothiophenols with mesityl oxide, and also with methyl-β-bromoisobutyl ketone, derivatives of dihydrobenzohepta-1,5-thiazine are formed.

Syntheses of new derivatives of heptathiazone are described below. o-Aminothiophenol, 5-nitro-2-aminothiophenol, N-methyl-, N-ethyl- and N-phenyl-o-aminothiophenols were used as amino components in the condensation. Of the unsaturated ketones the following were used for the reaction: mesityl oxide, ethylideneacetone and methylvinyl ketone. The formation of seven-membered, heterocyclic ring compounds from the aminothiols, not substituted at the nitrogen atom, proceeds according to the scheme:



R & R' = H, CH_3; X = H, NO_2.

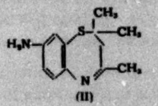
(I)

Condensation of the aminothiols takes place most easily with mesityl oxide. With ethylideneacetone and especially with methylvinyl ketone the yield of condensation products is considerably lower.

The nitro group in position 5 in the aminothiophenol retards the condensation reaction. Thus, for example, on condensation of 5-nitro-2-aminothiophenol with mesityl oxide the yield of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) (X = NO_2; R and R' = CH_3) is only 13%. As a rule the yield of heptathiazines increases when, instead of unsaturated ketones, the corresponding β-haloketones are used in the condensation with aminothiols, and this is particularly valuable for the condensation of nitroaminothiophenols. For example, on condensing 5-nitro-2-aminothiophenol with methyl-β-bromoisobutyl ketone the yield of the bromohydrate of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) (X=NO_2; R and R' = CH_3) exceeds 70%.

On condensing 6-nitro-2-aminothiophenol with ethylideneacetone we were completely unsuccessful in isolating the corresponding nitroheptathiazine. When methyl-β-bromopropyl ketone was used for this reaction the yield of the hydrobromide 2,4-dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) (X = NO_2; R = CH_3, R' = H) was 40%.

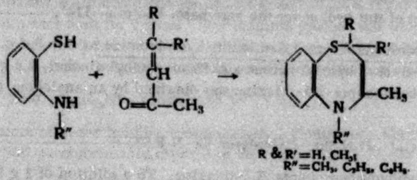
On reduction of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine with tin in hydrochloric acid, the corresponding amine 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine (II), was formed in 75% yield.



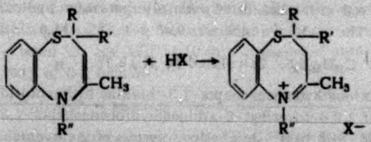
(II)

The same sort of qualitative difference in closing the seven-membered, heterocyclic ring is found with N-substituted o-aminothiophenols. Here also condensation with mesityl oxide proceeds easily. With methylvinyl ketone the yield of condensation products is quite insignificant.

The nature of the radical attached to the nitrogen atom of the aminothiols exerts a substantial effect on the yield of condensation products. It was established that the highest yield of heptathiazines is obtained when N-phenyl-o-aminothiophenol is used for condensation with unsaturated ketones. Thus, for example, on condensation of N-phenyl-o-aminothiophenol with methylvinyl ketone, the yield of base is 68%, whereas with the N-alkyl-o-aminothiophenols the yield of the corresponding heptathiazine base is only 16-30%.



When the bases obtained were heated with mineral acids, the quaternary salts were obtained in quantitative yields.



Usually the perchlorates, which can easily be isolated in the crystalline state, are obtained. The corresponding quaternary chlorides are obtained by saturating a benzene solution of the base with hydrogen chloride. These quaternary salts are difficult to crystallize. They form a glassy mass, deliquescing in the air. They are quite suitable for preparing cyanine dyes.

EXPERIMENTAL

2,4-Dimethyldihydrobenzohepta-1,5-thiazine. A mixture of 11.2 g o-aminothiophenol and 7.5 g of ethylideneacetone was heated in a sealed tube, on the water bath, for 3 hours. The reaction product was dissolved in ether, washed with aqueous alkali, dried over solid potassium hydroxide and redistilled in vacuo. 7.5 g, or 44%, of a fraction boiling at 125-128° and 5 mm was collected. In a repeated redistillation a fraction consisting of pure 2,4-dimethyldihydrobenzohepta-1,5-thiazine was collected.

B.p. 115-118° at 2 mm, d^{20}_{20} 1.1147, $n^{20}D$ 1.60683.

Found %: N 7.36; S 16.58. $C_{11}H_{13}NS$. Calculated %: N 7.33; S 16.75.

The picrate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was obtained by mixing equivalent quantities of alcoholic solutions of the base and of picric acid. The picrate, recrystallized from alcohol had m.p. 157°.

Found %: N 13.31, 13.41. $C_{17}H_{16}O_7N_4S$. Calculated %: N 13.33.

2,2,4-Trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine. A mixture of 3 g 5-nitro-2-aminothiophenol and 2 g of mesityl oxide was heated in a sealed tube for 3 hours at 130°. The reaction product was then dissolved in ether and washed with aqueous alkali. After the ether was evaporated the residue consisted of a dark resin which crystallized after addition of a few drops of alcohol and rubbing with a glass rod. The crystals were filtered off and recrystallized from alcohol. 0.6 g (13.6%) of pure 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine were obtained in the form of light-yellow prisms with m.p. 114°.

Found %: N 10.90, 10.82. $C_{12}H_{14}O_2N_2S$. Calculated %: N 11.10.

2,2,4-Trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide. A mixture of 10 g 5-nitro-2-aminothiophenol, 10 g freshly redistilled methyl-β-bromoisobutyl ketone and 100 ml methyl alcohol was heated on the water bath until all the nitroaminothiophenol went into solution. This required 15-20 minutes. The methyl alcohol was then evaporated down in an evaporating dish on the water bath to $^1/_3$ volume. The hydrobromide of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine crystallized out from the residue on cooling. Yield 13 g (71%); m.p. 188°. A furtherquantity of impure product could be isolated from the mother liquor.

Found %: N 8.38, 8.35; Br 23.90, 23.92. $C_{12}H_{15}O_2N_2SBr$. Calculated %: N 8.46; Br 24.11.

The base isolated from this salt was shown to be identical with 2,2,4-trimethyl-8-nitrodihydrobenzohepta-5-aminothiophenol. A mixture of the two, as for the pure base, had m.p. 114°.

2,4-Dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide. From 3.4 g 5-nitro-2-aminothiophenol, 3.3 g freshly redistilled methyl-β-bromopropyl ketone and 25 ml methyl alcohol, 2.5 g (39.4%) of the hydrobromide of 2,4-dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine was obtained by an analogous method, having m.p. (from alcohol) 186°.

Found %: N 8.87, 8.89. $C_{11}H_{13}O_2N_2SBr$. Calculated %: N 8.83.

2,2,4-Trimethyl-8-aminodihydrobenzohepta-1,5-thiazine. To a solution of 1 g 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide in 8 ml concentrated hydrochloric acid, was added 1.5 g granulated tin. After evolution of heat had ceased the mixture was heated on the water bath until the tin had completely dissolved. The crystalline precipitate that formed was decomposed with aqueous alkali to a strongly alkaline reaction. The amine was extracted with ether, dried over solid potassium hydroxide and recrystallized from alcohol after evaporating off the ether. The yield of amine was 0.45 g or 75%. M.p. 140°.

Found %: N 12.78, 12.73. $C_{12}H_{16}N_2S$. Calculated %: N 12.72.

2,2,4-Trimethyl-8-acetaminodihydrobenzohepta-1,5-thiazine hydrochloride. The hydrochloride prepared by saturating an ethereal solution of 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine with hydrogen chloride, was dissolved in acetic anhydride, with heat. On cooling, crystals of the hydrochloride of the acetyl derivative of the amine were deposited. M.p. 210°.

Found %: N 9.56, 9.52. $C_{14}H_{19}ON_2SCl$. Calculated %: N 9.40.

On adding ammonia to an aqueous solution of the hydrochloride of the acetyl derivative, free 2,2,4-trimethyl-8-acetaminodihydrobenzohepta-1,5-thiazine was obtained, having m.p. 150°.

Found %: N 10.63, 10.62. $C_{14}H_{18}ON_2S$. Calculated %: N 10.69.

2,4,5-Trimethyldihydrobenzohepta-1,5-thiazine. A mixture of 9.3 g N-methyl-o-aminothiophenol and 5.6 g ethylideneacetone was heated in a sealed tube on the water bath for 4 hours. The reaction product was extracted with ether, washed with alkali and redistilled in vacuo at 2 mm after evaporating off the ether. 6 g (43%) of a fraction boiling at 120-126° was collected. 2,4,5-Trimethyldihydrobenzohepta-1,5-thiazine is a colorless liquid; d^{20}_{20} 1.0909, $n^{20}D$ 1.5911.

Found %: N 6.66, 6.92. $C_{12}H_{15}NS$. Calculated %: N 6.83.

The methylperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was formed by mixing the base obtained with 30% perchloric acid. The quaternary salt, recrystallized from alcohol had m.p. 111°.

Found %: N 4.77; Cl 11.95. $C_{12}H_{16}O_4NSCl$. Calculated %: N 4.58; Cl 11.62.

The chloromethacrylate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was formed on saturating a benzene solution of the base with hydrogen chloride. This quaternary salt was obtained in the form of a glassy mass. It was not isolated in the crystalline state.

2,4-Dimethyl-5-ethyldihydrobenzohepta-1,5-thiazine. A mixture of 8 g N-ethyl-o-aminothiophenol and 4.5 g ethylideneacetone was heated on the water bath for 2 hours. The condensation product was then washed with alkali, extracted with ether and dried over solid potassium hydroxide. After evaporating off the ether the residue was redistilled in vacuo at 2 mm and 130-138°. The yield of 2,4-dimethyl-5-ethyldihydrobenzohepta-1,5-thiazine was 6 g (50%); d^{20}_{20} 1.0657; n_D 1.57078.

Found %: N 6.15; S 14.06. $C_{13}H_{17}NS$. Calculated %: N 6.11; S 14.00.

The ethylperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was obtained by mixing the base with 30% perchloric acid. The crystals of the quaternary salt which separated out were recrystallized from alcohol. The melting point of the quaternary salt was 170°.

Found %: N 4.39; Cl 11.32. $C_{13}H_{18}O_4NSCl$. Calculated %: N 4.38; Cl 11.11.

4,5-Dimethyldihydrobenzohepta-1,5-thiazine. On mixing 7.1 g N-methyl-o-aminothiophenol with 3.6 g methylvinyl ketone the mixture warmed up and formed an emulsion (as a result of the formation of water). The mixture was heated on the water bath for 2 hours. The reaction product was then dissolved in ether, washed with alkali, dried over solid potassium hydroxide and redistilled in vacuo. 2.9 g (30%) of a fraction boiling at 100-103° and 6 mm was collected. 4,5-Dimethyldihydrobenzohepta-1,5-thiazine is a colorless oil; d^{20}_{20} 1.0921, $n^{20}D$ 1.60143.

Found %: N 7.42; 7.30. $C_{11}H_{13}NS$. Calculated %: 7.33.

The methylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine. On mixing 4,5-dimethyldihydrobenzohepta-1,5-thiazine with 50% perchloric acid, crystals of the quaternary salt were formed, with m.p. 100.5°.

Found %: N 4.77, 4.43; Cl 12.20. $C_{11}H_{14}O_4NSCl$. Calculated %: N 4.79; Cl 12.18.

4-Methyl-5-ethyldihydrobenzohepta-1,5-thiazine. On mixing 7.2 g N-ethyl-o-aminothiophenol with 3.3 g methylvinyl ketone the mixture warmed up and formed an aqueous emulsion. After heating for 3 hours in a sealed tube on the water bath, the reaction product was washed with alkali and extracted with ether. The ethereal solution was dried over solid potassium hydroxide, the ether distilled off and the residue redistilled in vacuo. 1.6 g (16%) of a fraction collected between 125 and 130° at 10 mm consisted of pure 4-methyl-5-ethyldihydrobenzohepta-1,5-thiazine; d^{20}_{20} 1.1103, $n^{20}D$ 1.58223.

Found %: N 6.87, 6.90. $C_{12}H_{15}NS$. Calculated %: N 6.83.

The ethylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine was prepared by mixing 4-methyl-5-ethyldihydrobenzohepta- 1,5-thiazine with 50% perchloric acid. The quaternary salt isolated crystallized out after two days. Colorless crystals with m.p. 131°.

Found %: N 4.56, 4.50; Cl 11.63. $C_{12}H_{16}O_4NSCl$. Calculated %: N 4.58; Cl 11.62.

The chloroethylate of 4-methyldihydrobenzohepta-1,5-thiazine was prepared by saturating a benzene solution of the base with hydrogen chloride. This quaternary salt was a glassy mass, deliquescing in the air.

The condensation of N-phenyl-o-aminothiophenol with methylvinyl ketone. A mixture of 3 g N-phenyl-o-aminothiophenol and 1.1 g methylvinyl ketone was heated in a sealed tube on the water bath, for 3 hours. Drops of water appeared in the upper part of the tube. The condensation product was treated with alkali, extracted with ether, dried over solid potassium hydroxide and the ether distilled off on the water bath. The residue, weighing 3.2 g, was mixed with 50% perchloric acid. After rubbing with a glass rod, crystals of the phenylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine, weighing 3 g (68%), separated. M.p. 162-163°.

Found %: N 3.89, 3.93; Cl 9.83. $C_{16}H_{16}O_4NSCl$. Calculated %: N 3.96; Cl 10.04.

SUMMARY

1. By condensing α,β-unsaturated ketones and β-haloketones with o-aminophenylmercaptans the following new derivatives of dihydrobenzohepta-1,5-thiazine were obtained: 2,4-dimethyl-, 2,2,4-trimethyl-8-nitro-, 2,4-dimethyl-8-nitro-, 2,4,5-trimethyl-, 2,4-dimethyl-5-ethyl-, 4,5-dimethyl-, 4-methyl-5-ethyl- and 4-methyl-5-phenyldihydrobenzohepta-1,5-thiazine.

2. By reduction of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine, the corresponding amine, 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine, was obtained.

3. From N-alkyl and N-phenyldihydrobenzohepta-1,5-thiazines and mineral acids, the following quaternary salts of dihydrobenzohepta-1,5-thiazine were obtained in quantitative yields: the methylperchlorate of 2,4-dimethyl-, the ethylperchlorate of 2,4-dimethyl, the methylperchlorate of 4-methyl-, the ethylperchlorate of

4-methyl- and the phenylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine.

Received January 28, 1957 Kiev State University

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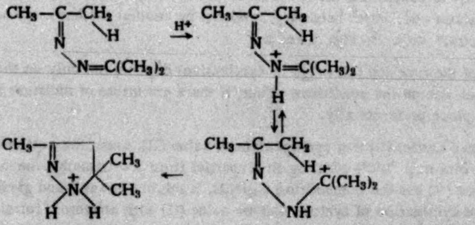
THE REACTIONS OF HYDRAZINE DERIVATIVES

XVIII. THE ACTION OF ACIDIC REAGENTS ON AZINES

A. N. Kost, I. I. Grandberg and E. B. Evreinova

The conversion of azines to pyrazolines under the action of acids [1, 2] or alkyl halides [3, 4] has been reported in a number of previous communications.

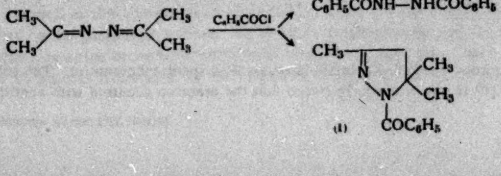
The mechanism of this cyclization is evidently analogous to the mechanism of the aldol condensation. In the formation of aldols (in acid media) the first step is the addition of a proton to the oxygen of the carbonyl group, with the formation of a carbocation. The latter reacts with a second molecule of aldehyde and then splits off the proton. Similarly azines readily take up a proton, the ammonium ion isomerizing to carbonium, thus making cyclization possible. In contrast to the aldol condensation the proton does not split off at the end of the reaction because of the formation of a stable pyrazoline ion.



Information on the action of acyl halides on azines is extremely contradictory. Thus, Minunni [5] observed that benzaldazine, under the action of benzoyl chloride, is converted to benzaldehyde benzoylhydrazone, but furfural azine breaks down, giving dibenzoylhydrazine. On the other hand Lochte [6] reported that acetone azine cyclizes with the same reagent, to form 1-benzoyl-3,5,5-trimethylpyrazoline (I). According to the data of Benary [7] cyclohexanone azine is converted, by the action of acyl halides, to the 1-acyloctahydrocarbazole (with splitting off of ammonia). Finally, it is stated that acetophenone azine does not react with acyl halides [7].

We have confirmed Benary's findings as regards the conversion of cyclohexanone azine to the octahydrocarbazole but we were unable to extend this reaction to other azines (with the object of synthesizing homologs of pyrrole).

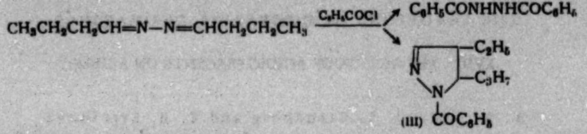
From acetone azine and benzoyl chloride we obtained a substance with m.p. 236°, identical with that described by Lochte, but it proved to be not benzoylpyrazoline (I), but sym-dibenzoylhydrazine. However benzoylpyrazoline (I) can be obtained by the action of benzoylchloride on acetone azine in the total absence of moisture, but this substance has completely different properties (m.p. 93°) and was characterized by us for the first time [8].



(I)

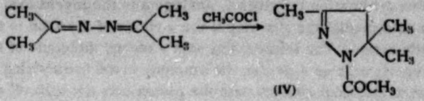
We have found a similar phenomenon (the cleavage of azines with the formation of sym-diacylhydrazines) by the action of benzoyl chloride on the azines of methylisopropyl ketone and cyclopentanone (II).

By the action of benzoyl chloride on butyraldazine (as for acetone azine), 1-benzoyl-4 ethyl-5-propylpyrazoline (III) was obtained together with dibenzoylhydrazine.



(III)

Cyclopentanone azine (II) reacts exothermically with acetyl chloride, but in this case we succeeded in isolating only sym-diacetylhydrazine. With acetone azine, on the other hand, only the product of cyclization was obtained, i.e., 1-acetyl-3,5,5-trimethylpyrazoline (IV).

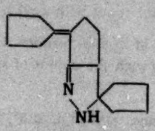


(IV)

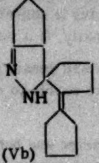
For the purpose of confirming the structure of the compounds formed, in addition to elementary analysis, comparison of constants and, where necessary, synthesis by another method, we characterized the substances by the absorption spectra,* shown in Figs. 1 and 2.

The course of the reaction (cleavage or cyclization) depends not only on the nature of the azine and the acylating agent, but also on the conditions. Thus, if there are traces of moisture in the reaction mixture, cleavage of the azine takes place preferentially.

We have stated earlier [9] that cyclopentanone azine (II), under the action of oxalic acid, is converted to the compound (V) with m.p. 140°, differing in properties from 3,4-trimethylene-5,5-tetramethylene pyrazoline (VI). This substance (V) has the composition $C_{15}H_{22}N$, is soluble in acids and gives picrate and benzoyl derivatives. On carrying out the cyclization of cyclopentanone azine (II) with anhydrous formic acid,** the same substance (V) was isolated together with cyclopentanone formylhydrazone (VII). In contrast to the absorption spectrum of the pyrazoline (VI) the absorption maximum in the spectrum of substance (V) is displaced toward the red end of the spectrum (Fig. 3), which can be explained by the presence of a conjugated system of double bonds. From these considerations we consider that substance (V) has the structure (Va) or (Vb), the former being the more probable.



(Va)



(Vb)

Evidently the pyrazoline (VI), formed initially from cyclopentanone azine (II), under the action of the acidic reagent, enters into a crotonic type condensation with a second molecule of the azine (in a manner analogous to that taking place with aldimines [10]), whereupon, in the case of formic acid the hydrazone formylates.

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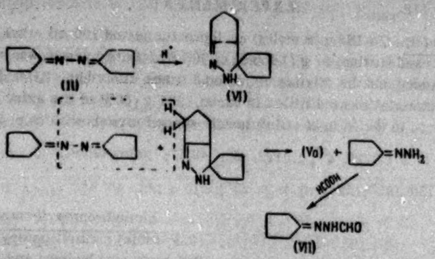
* The spectra were recorded by N. B. Kupletskaia on an SF-4 spectrophotometer. The solvent was methyl alcohol.

** In a previous paper [9] it was erroneously stated that the reaction occurred with acetic acid.



On attempting to decompose the pyrazoline (V) by the method of Kirschner we did not succeed in obtaining the corresponding cyclopropane hydrocarbon, having a double carbon-carbon bond, conjugated with the four-membered ring (much resinification occurred).

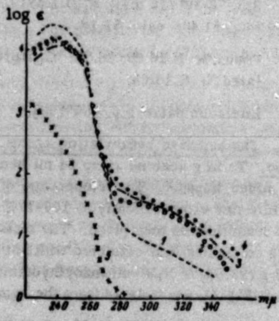


Fig. 1. Absorption spectra of 1-acyl-3,5,5-trimethylpyrazolines. 1) 1-acetyl-(λ_{max} 236 mμ, log ε 4.403); 2) 1-propionyl-(λ_{max} 239 mμ, log ε 4.135); 3) 1-butyryl-(λ_{max} 239 mμ, log ε 4.117); 4) 1-isovaleryl-(λ_{max} 239 mμ, log ε 4.134); 5) sym-dibenzoylhydrazine.

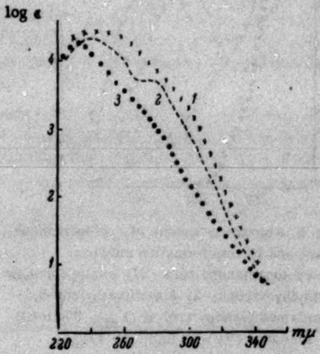


Fig. 2. Absorption spectra of 1-benzoylpyrazolines. 1) 1-benzoyl-3,5,5-trimethylpyrazoline (λ_{max} 247 mμ, log ε 4.348); 2) 1-benzoyl-4-ethyl-5-propylpyrazoline (λ_{max} 235-238 mμ, log ε 4.255); 3) sym-dibenzoylpyrazoline (λ_{max} 232 mμ, log ε 4.279).

It is interesting that the crystals of substance (V), the molecule of which is clearly symmetrical, possess a strong piezoelectric effect, almost equal to that of quartz (according to data provided by V. A. Koptsik[*]).

While investigating the action of various acidic reagents on azines we noticed that cyclohexanone azine reacts vigorously with phosphorus tribromide. We tried to moderate the conditions and carried out the reaction in dioxan. Unexpectedly, as well as the octahydrocarbazole [11], β,β'-dibromodiethyl ether (bromex) was obtained in good yield (calculated on the phosphorus tribromide), being formed by opening of the dioxan ring. Without the addition of cyclohexanone azine or with the addition of other bases, we either failed to obtain Bromex from dioxan by the action of phosphorus tribromide, or the yield was very small. Phosphorus trichloride under these conditions does not cyclize cyclohexanone azine and does not give Chlorex.

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[*] Faculty of Physics, Moscow State University.

EXPERIMENTAL

Cyclopentanone azine (II). To 168 g (2 moles) cyclopentanone and 100 ml ethyl alcohol, with external cooling (0-2° in the mixture) and stirring, 52 g (1 mole) of 96% hydrazine hydrate was added dropwise. After 1-2 hours 150 g potash was added and the mixture extracted 3 times with ether. After drying over potash and distilling of the solvent the material was redistilled in vacuo. 131 g (80%) of the azine (II) was obtained. On standing, the azine crystallized in the form of white, needle-shaped crystals with m.p. 24-24.5°.

B.p. 118.5° (14 mm), $n^{20}D$ 1.5222, d^{20}_4 1.0122, MR_D 49.51; calc. 49.69.

Literature data: b.p. 130-132° (22 mm), m.p. 25° [12].

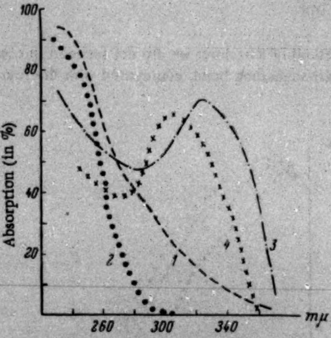

Fig. 3. Absorption spectra of cyclopentanone azine and its transformation products.
1) cyclopentanone azine; 2) cyclopentanone formylhydrazone; 3) 3,4-trimethylene-5,5-pentamethylenepyrazoline (λ_{max} 324 mμ); 4) substance (V) with m.p. 140° (λ_{max} 304 mμ).

Methylisopropylketazine. A mixture of 72.5 g (0.85 mole) methylisopropylketone, 21.3 g (0.43 mole) 96% hydrazine hydrate and 20 ml alcohol was boiled under reflux for 10 hours. 25 g potash was then added and the mixture extracted twice with ether. After drying over magnesium sulfate and redistilling twice, in vacuo, 50 g (70%) of methylisopropylketazine was obtained.

B.p. 78-79° (16 mm), $n^{20}D$ 1.4519, d_{20} 0.8728, MR_D 51.46; calc. 51.18.

Found %: N 16.69, 16.77. $C_{10}H_{20}N_2$. Calculated %: N 16.65.

Literature data: b.p. 165° [13].

The action of benzoylating agents on acetone azine. To 22 g acetone azine 24 ml benzoyl chloride was added dropwise. The temperature of the reaction mixture rose exothermically to 100-110° and considerable resinification took place. The mass, which crystallized on cooling, was extracted with hot benzene. 15.3 g (93.8%) of N,N'-dibenzoylhydrazine, with m.p. 237-238° [14], was isolated from the benzene solution.

Found %: N 11.61, 11.66. $C_{14}H_{12}O_2N_2$. Calculated %: N 11.66.

Absorption spectrum (in alcohol): λ_{max} 232 mμ, log ε 4.279.

When the reaction was carried out with careful exclusion of moisture, evolution of hydrogen chloride took place. On vacuum distillation benzoic acid and 1-benzoyl-3,5,5-trimethylpyrazoline (I) was isolated. Yield 12.4%.

B.p. 145-147° (6 mm), m.p. 92-93° [8]. Absorption spectrum (in alcohol): λ_{max} 247 mμ, log ε 4.348.

Found %: C 71.87, 71.96; H 7.67, 7.72. $C_{13}H_{16}ON_2$. Calculated %: C 72.19, H 7.45.

Similarly, to 11.2 g acetone azine 22.6 g benzoic anhydride in 25 ml anhydrous benzene was added, with stirring. After 1 hour the solvent was distilled off and from a fraction collected (b.p. 51-93°) acetone semicarbazone, with m.p. 185-186°, was obtained by the action of semicarbazide. The residue in the flask was washed three times with hot 2 N sodium hydroxide solution, yielding 2.2 g benzoic acid (m.p. 121-122°, giving no melting point depression with a pure sample) and 18 g (75%) N,N'-dibenzoylhydrazine with m.p. 234-238°, λ_{max} 231-232 mμ.

The reaction of acetone azine with acetyl chloride. 11.2 g of the freshly redistilled azine was added dropwise, with continuous stirring and external cooling, to 50 ml of freshly redistilled acetyl chloride. After 2.5 hours, without cessation of stirring, the mixture was heated to 75° and after 20 minutes the temperature was raised to 100°. The excess acetyl chloride was then distilled off; the residual oil crystallized out. On recrystallizing from petroleum ether, colorless, cubic crystals of 1-acetyl-3,5,5-trimethylpyrazoline (IV), were obtained. Yield 7.4 g (49%), m.p. 44.5° [4]. No depression of melting point was given with a sample obtained by the action of excess acetic anhydride on 3,5,5-trimethylpyrazoline at −5°. Yield 83%, m.p. 44-45°, λ_{max} 236 mμ, log ϵ 4.403.

The reaction of butyraldazine with benzoyl chloride. 18 ml benzoyl chloride was added to 14 g butyraldazine. After exothermal reaction had ceased the mixture was heated on the water-bath under reflux for 1.5 hours, treated with 100 ml water and extracted with 50 ml ether. White crystals of N,N'-dibenzoylhydrazine, with m.p. 236-238°, then separated out. Yield 2.7 g (22.5%), λ_{max} 232 mμ. From the ethereal extract, after drying over potash and redistilling, 3 g (16%) 1-benzoyl-4-ethylpropylpyrazoline (III) was obtained.

B.p. 210-215° (17 mm), $n^{20}D$ 1.5690 [8].

Absorption spectrum: λ_{max} 238 mμ, log ϵ 4.255.

The reaction of methylisopropylketazine with benzoyl chloride. 5.1 g of the azine of methylisopropylketone was added dropwise, with shaking, to 8.4 g of freshly redistilled benzoyl chloride. An exothermal reaction and partial resinification occurred. The resulting mass was poured into 150 ml of 2 N sodium hydroxide solution. The crystals of dibenzoylhydrazine deposited were washed with sodium hydroxide solution and hot water. Yield: 5.3 g (74%), m.p. 232-236°. 3.8 g benzoic acid was isolated from the wash water after acidification. Attempts to carry out cyclization of the azine of methylisopropylketone with formic or oxalic acids were not successful (either extensive resinification occurred or the azine was recovered unchanged).

The reaction of cyclopentanone azine (II) with acyl halides. 9.2 g acetyl chloride was added in small portions to a solution containing 8.2 g of the azine (II) in 50 ml ether, with external cooling (solution temperature 5°) and stirring. The precipitated N,N'-diacetylhydrazine was filtered off and dried in a vacuum desiccator over phosphoric anhydride. Yield 4.2 g (72%) m.p. 139-140° [15].

Similarly, from 8.2 g of the same azine and 15 ml benzoyl chloride in 50 ml benzene (without cooling), 23 g of a brown resinous mass was obtained, from which, after extraction with 5 N aqueous sodium hydroxide, followed by acidification with hydrochloric acid and recrystallization from absolute alcohol, 2.5 g (21%) of N,N'-dibenzoylhydrazine, m.p. 232-234° was obtained.

The reaction of cyclopentanone azine (II) with oxalic acid. 32.8 g of the azine (II) was mixed with 27 g of carefully ground, anhydrous oxalic acid and allowed to stand for three days at room temperature. The viscous mass was decomposed by the addition of 500 ml of 2N aqueous potassium hydroxide solution. The deposited crystals of substance (V), after separation, were washed with water, dried in a vacuum desiccator and recrystallized 6 times from benzene; m.p. 140°. Yield 26 g (66%).

Found %: C 77.98, 78.09; H 9.70, 9.64; N 12.28, 12.39. $C_{15}H_{22}N_2$. Calculated %: C 78.26; H 9.54; N 12.18.

The substance is soluble in dilute hydrochloric acid and can be recovered by addition of alkali. Darkens on prolonged standing in air. Decomposes under the action of oxidizing agents, with evolution of nitrogen.

Picrate, m.p. 176.5° (from alcohol).

Found %: N 15.32, 15.39. $C_{21}H_{25}O_7N_5$. Calculated %: N 15.24.

Benzoyl derivative m.p. 181° (from methyl alcohol).

Found %: C 79.33, 79.21; H 7.80, 7.91; N 8.44, 8.59. Calculated %: C 79.00; H 7.83; N 8.38.

If the reaction between the azine (II) and oxalic acid is carried out at 50° for 1 hour, after treatment with alkali and distillation of the benzene extract, 55% of unchanged azine (II) and 30% substance (V), b.p. 180° (6 mm), m.p. 140° (from benzene) are obtained.

The reaction of cyclopentanone azine (II) with formic acid. 32.8 g of the azine (II) was mixed with 13.8 g of anhydrous formic acid. After 6 hours (at room temperature) the viscous, partially crystallized oil was decomposed with 300 ml of 2N sodium hydroxide solution. The crystals deposited were separated, by crystallizing twice from benzene, into substance (V), m.p. 139-140°, identical with that described in the previous experiment (giving no mixed melting point depression), and cyclopentanone formylhydrazone (VII), m.p. 125.5-126°.

Found %: C 57.24, 57.40; H 8.05, 8.12; N 22.36, 22.48. $C_6H_{10}ON_2$. Calculated %: C 57.15; H 7.99; N 22.22.

This same substance, with m.p. 127° (from benzene), giving no mixed melting point depression with that described above, was obtained by refluxing equivalent quantities of cyclopentanone and formylhydrazine, in alcoholic solution for 2 hours.

The reaction of dioxan with phosphorus tribromide in the presence of cyclopentanone azine. A mixture of 39.2 g cyclopentanone azine, 55 g phosphorus tribromide and 70 ml dioxan was heated to boiling for 2 hours. At the end of the reaction the reaction mixture was poured into water and the heavy layer that separated washed with sodium carbonate, dilute hydrochloric acid, and water; dried over calcium chloride and redistilled in vacuo. 32.7 g (69%) of β,β'-dibromodiethyl ether was obtained.

B.p. 123.5° (47 mm), $n^{20}D$ 1.5125, d^{20}_4 1.8452, MR_D 37.76; calc. 37.84.

Found %: C 20.88, 21.00; H 3.64, 3.61. $C_4H_8OBr_2$. Calculated %: C 20.68; H 3.45.

Literature data: b.p. 115° (32 mm); $n^{20}D$ 1.5131, d^{20}_4 1.8222 [16].

In addition 12 g (30%) of octahydrocarbazole, b.p. 158-166° (13-14 mm), m.p. 87° [11], was isolated.

No Bromex was obtained by boiling dioxan with phosphorus tribromide for 2 hours. In the presence of pyridine the yield of Bromex was 34%; when triethylamine was used the yield fell to nil. Phosphorus trichloride under analogous conditions did not bring about the formation of Chlorex.

SUMMARY

1. The action of acyl halides on azines has been investigated. It was found that, depending on the conditions and the structure of the azine, the latter either broke down with the formation of the sym-diacylhydrazine, or cyclized to the 1-acylpyrazoline.

2. The structure of the substance formed by the action of acidic reagents on cyclopentanone azine has been investigated.

Received February 7, 1957

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*Original Russian pagination. See C. B. Translation.

DERIVATIVES OF HEXAMETHYLENIMINE

III. SUBSTITUTED N-BENZYLHEXAMETHYLENIMINES

G. S. Kolesnikov and L. I. Shcherbo

The synthesis of aliphatic N-substituted hexamethylenimine derivatives was described previously [1]. Continuing our investigation of the synthesis of hexamethylenimine derivatives, we undertook the synthesis of substituted N-benzylhexamethylenimines, which are hexamethylenimine derivatives containing an aliphatic-aromatic substituent on the nitrogen atom. These compounds were prepared by reacting hexamethylenimine with benzyl halides, containing substituents in the nucleus; we chose fluorine, chlorine and bromine as substituents.

$$(CH_2)_6NH + ArCH_2X \rightarrow (CH_2)_6NCH_2Ar + HX$$

The hydrogen halide formed was bound with hexamethylenimine, of which a sufficient excess was used to combine with all the hydrogen halide formed [1, 2]. The synthesis was carried out by the method described previously [1]. The substituted N-benzylhexamethylenimines were characterized as their picrates. The results obtained are given in the table.

Substituted N-benzylhexamethylenimines with the General Formula $(CH_2)_6NCH_2Ar$

CH_2Ar	Yield (in %)	Boiling point (pressure in mm)	d_{20}^{20}	n_D^{25}
Benzyl	77	145—146° (3)	0.9657	1.5280
o-Fluorobenzyl	50	138—141 (3—4)	1.0340	1.5158
o-Chlorobenzyl	42	136—139 (5)	1.0950	1.5425
m-Chlorobenzyl	47	149—150 (8)	1.0740	1.5104
p-Fluorobenzyl	51	135—136 (15)	1.0430	1.5122
p-Chlorobenzyl	50	162—163 (11—12)	1.0750	1.5109
p-Bromobenzyl	51.5	160—162 (3—4)	1.2640	1.5580

EXPERIMENTAL

N-Benzylhexamethylenimine. From 157 g of hexamethylenimine and 100 g of benzyl chloride in 150 ml of benzene we obtained 101 g of N-benzylhexamethylenimine.

Found : M 190.5; 189.1. $C_{13}H_{19}N$. Calculated : M 189.3.

Picrate, m.p. 145-147° (from alcohol).

Found %: N 13.31; 13.13. $C_{19}H_{22}O_7N_4$. Calculated %: N 13.39.

N-o-Fluorobenzylhexamethylenimine. o-Toluidine was converted, via the diazonium fluoborate, into o-fluorotoluene in 41% yield and the latter had b.p. 112-116°. Bromination at 80-110° converted the o-fluorotoluene into o-fluorobenzyl bromide; the yield was 60% and the b.p. 195-200°. From 30 g of hexamethylenimine and 30 g of o-fluorobenzyl bromide in 50 ml of benzene we obtained 22 g of N-o-fluorobenzylhexamethylenimine.

Found : M 211.8, 207.2. $C_{13}H_{18}NF$. Calculated: M 207.15.

Picrate, m.p. 135-136° (from alcohol).

Found %: N 12.65; 12.64. $C_{19}H_{21}O_7N_4F$. Calculated %: N 12.84.

N-o-Chlorobenzylhexamethylenimine. o-Toluidine was converted via the diazo compound into o-chlorotoluene in 56% yield and the latter had b.p. 156-159°. Bromination at 110° yielded o-chlorobenzyl bromide; the yield was 67% and the b.p. 112-114° at 10 mm. From 56 g of hexamethylenimine and 50 g of o-chlorobenzyl bromide in 100 ml of benzene we obtained 25.5 g of N-o-chlorobenzylhexamethylenimine.

Found: M 221.0; 217.0. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 137-139° (from alcohol).

Found %: N 12.53; 12.78. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-m-Chlorobenzylhexamethylenimine. From 58 g of hexamethylenimine and 46 g of m-chlorobenzyl chloride in 100 ml of benzene we obtained 30 g of N-m-chlorobenzylhexamethylenimine.

Found: M 214.0; 216.8. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 152-154° (from alcohol).

Found %: N 12.37, 12.53. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-p-Fluorobenzylhexamethylenimine. p-Toluidine was converted via the diazonium fluoborate into p-fluorotoluene in 25.8% yield and the latter had b.p. 114-116°. Bromination of p-fluorotoluene at 80-110° yielded p-fluorobenzyl bromide; the yield was 75.6% and the b.p. 195-200°. From 63 g of hexamethylenimine and 60 g of p-fluorobenzyl bromide in 100 ml of benzene we obtained 45 g of N-p-fluorobenzylhexamethylenimine.

Found: M 203.9, 201.2. $C_{13}H_{18}NF$. Calculated: M 207.15.

Picrate, m.p. 152-154° (from alcohol).

Found %: N 13.04, 13.01. $C_{19}H_{21}O_7N_4F$. Calculated %: N 12.84.

N-p-Chlorobenzylhexamethylenimine. From 76 g of hexamethylenimine and 60 g of p-chlorobenzyl chloride in 150 ml of benzene we obtained 48.1 g of N-p-chlorobenzylhexamethylenimine.

Found: M 217.0, 218.1. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 136-137° (from alcohol).

Found %: N 12.29, 12.05. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-p-Bromobenzylhexamethylenimine. By bromination at 120°, p-bromotoluene was converted into p-bromobenzyl bromide; the yield was 70.5%. From 60 g of hexamethylenimine and 77 g of p-bromobenzyl bromide in 100 ml of benzene we obtained 42.6 g of N-p-bromobenzylhexamethylenimine.

Found: M 274.2, 267.1. $C_{13}H_{18}NBr$. Calculated: M 268.5.

Picrate, m.p. 153-155° (from alcohol).

Found %: N 11.26, 11.24. $C_{19}H_{21}O_7N_4Br$. Calculated %: N 11.27.

SUMMARY

We prepared 7 substituted N-benzylhexamethylenimines, 6 of which are described for the first time.

Received February 13, 1957

Moscow Insitute of Chemical Technology

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF SOME AMINOALKYL ETHERS WITH CHOLINOLYTIC PROPERTIES

S. G. Kuznetsov and Z. I. Bobysheva

In searching for cholinolytic preparations, we decided to synthesize aminoalkyl ethers, similar in chemical structure to active cholinolytic substances in the aminoalkyl ester class. Of these, the diethylaminoethyl (I) and dimethylaminoethyl (II) esters are of particular interest, the former is known in American pharmacological literature under the symbol WIN 5606.

$$\underset{\text{(I)}}{(C_6H_5)_2C(OH)CO{-}O{-}CH_2CH_2N(C_2H_5)_2} \qquad \underset{\text{(II)}}{(C_6H_5)_2C(OH)CO{-}O{-}CH_2CH_2N(CH_3)_2}$$

$$\underset{\text{(III)}}{(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(C_2H_5)_2} \qquad \underset{\text{(IV)}}{(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(CH_3)_2}$$

It seemed interesting to synthesize the two aminoalkyl ethers (III) and (IV), which are analogous to the two esters mentioned above. The substitution of the CO group in these compounds by a methylene group must substantially affect their physical and chemical properties, in particular, polarity, solubility, basicity and stability to hydrolysis. It was natural to expect that changes in the physicochemical properties would also affect the cholinolytic activities of the compounds; however, it was difficult to forsee the character and, especially, the degree of change in the properties. The synthesis of these substances and a study of their pharmacological properties could help solve the problem of the relation between chemical structure and physiological activity in this group of compounds.

As the formulas given above show, the compounds we were interested in, (III) and (IV), are partial ethers of unsymmetrical diphenylethylene glycol and diethyl- or dimethylaminoethanol. We first tried using these substances to prepare compounds (III) and (IV).

Danilov [1] prepared unsymmetrical diphenylethylene glycol by reducing diphenylglycolaldehyde. The epichlorohydrin of this glycol was first synthesized by reacting phenylmagnesium bromide with ethyl chloroacetate [2] and then by reacting the chloroacetophenone with phenyllithium [3].

Having prepared the epichlorohydrin of unsymmetrical diphenylethylene glycol, we tried to carry out the following reaction.

$$(C_6H_5)_2C(OH)CH_2Cl + NaOCH_2CH_2N(C_2H_5)_2 \longrightarrow$$
$$\longrightarrow NaCl + (C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(C_2H_5)_2$$

However, the reaction did not proceed in the required direction as under the effect of alkaline agents, such as sodium β-diethylaminoethylate, in particular, this epichlorohydrin was very readily converted to unsymmetrical diphenylethylene oxide.

We synthesized the required aminoalkyl ethers in the following way:

$$ClCH_2COOC_2H_5 + NaOCH_2CH_2N(R)_2 \rightarrow C_2H_5OCOCH_2{-}O{-}CH_2CH_2N(R)_2 \rightarrow$$
$$\xrightarrow{2C_6H_5Li} \underset{R=CH_3,\ C_2H_5}{(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(R)_2}$$

Ethyl chloracetate reacted with sodium β-diethylaminoethylate in benzene solution to give a 20-22% yield of ethyl β-diethylaminoethoxyacetate and, in addition, a substance with a higher boiling point which was, apparently, the β-diethylaminoethyl ester of β-diethylaminoethoxyacetic acid. The formation of this substance may be explained by the side reaction of transesterification of ethyl chloroacetate and ethyl β-diethylaminoethoxyacetate. Ethyl chloroacetate also reacted with sodium β-dimethylaminoethylate in a similar way.

The second state of the synthesis — the reaction of the substituted acetate with phenyllithium — was carried out under the usual conditions for organolithium synthesis, namely, in an ether solution, without moisture, in an atmosphere of nitrogen and with cooling. The aminoalkyl ethers (III) and (IV) obtained by this reaction were purified by high vacuum distillation, then converted into hydrochlorides and recrystallized in this form. The yield of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III) was 70% and that of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (IV) was 56%.

We tried to prepare some derivatives of these aminoalkyl ethers. Heating (IV) with ethyl chloride in an acetone solution gave a 53% yield of the corresponding chloroethylate (V).

$$\underset{\text{(V)}}{(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(CH_3)_2(C_2H_5)Cl}$$

This compound is interesting in that its chemical structure is analogous to the very active cholinolytic substance — lachesin (VI) — which is well known abroad.

$$\underset{\text{(VI)}}{(C_6H_5)_2C(OH)CO{-}O{-}CH_2CH_2N(CH_3)_2(C_2H_5)Cl}$$

We also tried to prepare some derivatives of the aminoalkyl ethers (III) and (IV), using the hydroxyl groups in their molecules, and in particular, their chloro and acetyl derivatives. However, either the reaction did not proceed, as was the case, for example, when acetic anhydride or acetyl chloride were used, or proceeded with the elimination of a water molecule and the formation of the corresponding unsaturated compound, as was the case for example, when 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III was treated with thionyl chloride. In this case a 70% yield of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene (VII) was obtained and its structure was confirmed by a quantitative determination of the double bond and analysis for nitrogen and chlorine content (of the hydrochloride).

$$\underset{\text{(III)}}{(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(C_2H_5)_2} \xrightarrow{SOCl_2}$$

$$\longrightarrow \underset{\text{(VII)}}{(C_6H_5)_2C{=}CH{-}O{-}CH_2CH_2N(C_2H_5)_2} + H_2O$$

The aminoalkyl ethers (III), (IV), (V) and (VII) obtained were investigated pharmacologically and as a result it was established that these compounds have a definite cholinolytic activity, but to a considerably lesser degree than the aminoalkyl esters which correspond to them. The most active was a quaternary ammonium derivative of ether (V) and the least active was the unsaturated compound (VII).

One should add that after finishing this work, the report by Parkes [4] appeared in the literature giving the results of the pharmacological investigation of a series of aminoalkyl thioethers and ethers and the two ethers, (III) and (IV), obtained by us, are mentioned among them; however, the author does not indicate by what method and by whom and when these compounds were prepared. No information has as yet been published in the chemical literature on the substances synthesized by us.

EXPERIMENTAL

Ethyl β-diethylaminoethoxyacetate. 11.5 g of sodium was dissolved by heating in 64.3 g of β-diethylaminoethanol. The cooled reaction mixture was diluted with 25 ml of dry benzene and then a solution of 61.25 g of ethyl chloroacetate in 25 ml of benzene wasadded to it at 10-15°. The mixture was kept at room temperature for 2 hours and then at 40° for 1 hour. The whole process was carried out in an atmosphere of hydrogen. Carbon dioxide was passed into the reaction mixture to decompose the remaining alcoholate and then a sufficient amount of water was added to dissolve the precipitate of sodium chloride completely. The benzene layer was separated and the aqueous layer saturated with potassium carbonate and extracted with benzene. The combined benzene extracts were dried with potassium carbonate, the benzene distilled off and the residue vacuum distilled. Three fractions were obtained:

1st fraction – unreacted β-diethylaminoethanol with b.p. 42° (2 mm), 15.9 g; 2nd fraction – ethyl β-diethylaminoethoxyacetate with b.p. 85-86° (2 mm), 22.9 g and a 3rd fraction – apparently, the β-diethylaminoethyl ester of β-diethylaminoethoxyacetic acid with b.p. 128° (2 mm), 3.2 g. A second distillation of the 2nd fraction gave 13.2 g of ethyl β-diethylaminoethoxyacetate. It was a colorless, mobile liquid with the characteristic smell of aliphatic amines. It was readily soluble in water and most organic solvents.

B.p. 79-81° at 2 mm, $n^{20}D$ 1.4339, d^{20}_4 0.9566, MR_D 55.35; calc. 55.62.

Found %: N 6.78, 6.86. $C_{10}H_{21}NO_3$. Calculated %: N 6.89.

Ethyl β-dimethylaminoethoxyacetate was prepared similarly from 8.7 g of sodium, 72.6 g of β-dimethylaminoethanol and 46.5 g of ethyl chloroacetate.

B.p. 75-78° at 2 mm, $n^{20}D$ 1.4285, d^{20}_4 0.9801, MR_D 46.32, calc. 46.38.

Found %: N 7.85, 7.96. $C_8H_{17}NO_3$. Calculated %: N 8.00.

1,1-Diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III). A solution of phenyllithium, prepared in the usual way from 2.3 g of lithium and 23.6 g of bromobenzene in 100 ml of absolute ether, was treated at about 0° with a cooled solution of 10.1 g of ethyl β-diethylaminoethoxyacetate in 60 ml of ether. After standing at room temperature for 15-20 hours, the reaction mixture was decomposed with ice water, the ether layer separated and the aqueous layer extracted with ether. The combined ether extracts were treated with dilute hydrochloric acid. The acid aqueous extract was made alkaline with potassium carbonate. Free 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 precipitated in the form of an oily liquid and was extracted with ether. After being dried with potassium carbonate, the ether was distilled off and the residue distilled in high vacuum. We collected a fraction with b.p. 130° at 0.006 mm, which crystallized on standing. The yield was 10.9 g (70%). The colorless crystals (from petroleum ether) with m.p. 55-57° were readily soluble in organic solvents and difficultly soluble in water.

Found %: N 4.43, 4.25; OH 5.92, 5.76. $C_{20}H_{27}O_2N$. Calculated %: N 4.47; OH 5.42.

The hydrochloride of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 formed colorless crystals (from a mixture of anhydrous alcohol and ether) with m.p. 181-182°.

Found %: Cl 9.76, 10.01. $C_{20}H_{28}O_2NCl$. Calculated %: C 10.13.

1,1-Diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (IV) was prepared similarly from 3.5 g of ethyl β-dimethylaminoethoxyacetate and a solution of phenyllithium, prepared from 1 g of lithium and 11 g of bromobenzene. The yield was 3.2 g (56%). The thick oily liquid had b.p. 145° at 0.03 mm.

The hydrochloride of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 formed a colorless crystalline powder with m.p. 169-170° (from a mixture of alcohol and ether).

Found %: Cl 10.73, 10.89; N 4.19, 4.44. $C_{18}H_{24}O_2NCl$. Calculated %: Cl 11.02; N 4.35.

Chloroethylate of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (V). This was prepared by heating 1.72 g of (IV) with 8.5 ml of acetone and 6 ml of ethyl chloride for 6 hours at 65-70° in a sealed tube. The colorless crystals (from a mixture of alcohol and acetone) had m.p. 140-142°. The yield was 0.95 g (44%).

Found %: Cl 9.73, 9.86; N 4.10. $C_{20}H_{28}O_2NCl$. Calculated %: Cl 10.13; N 4.00.

The hydrochloride of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene. To a solution of 3.5 g of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 hydrochloride in 20 ml of chloroform was added 2 ml of thionyl chloride, diluted with 5 ml of chloroform and the mixture heated at 40-45° for 2 hours. After removal of the solvent in vacuum, the residue was recrystallized from a mixture of alcohol and ether. The colorless crystals had m.p. 142-144°. The yield was 2.3 g (70%).

Found %: Cl 10.56, 10.76. Bromine number 45.9, 43.9. $C_{20}H_{26}ONCl$. Calculated %: Cl 10.68. Bromine number 48.1.

SUMMARY

1. By reacting the ethyl chloroacetate with sodium β-dimethylaminoethylate and with sodium β-diethylaminoethylate we synthesized ethyl β-dimethylaminoethoxyacetate and ethyl β-diethylaminoethoxyacetate.

2. Reaction of phenyllithium with these esters gave 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 and 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1. The hydrochlorides of both these compounds and the chloroethylate of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 were prepared.

3. Dehydration of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 by treatment with thionyl chloride gave 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene.

Received January 23, 1957

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INVESTIGATION OF THE HYDROGEN BOND IN SOME CHOLINOLYTIC SUBSTANCES USING INFRARED ABSORPTION SPECTRA

S. G. Kuznetsov and V. N. Nikitin

The considerable effect that a hydrogen bond has on the physical and chemical properties of a substance is well known. Some also believe that the formation of a hydrogen bond may play an important part in the mechanism of physiological activity of a series of substances, among them medicinal, selectively toxic and other materials [1-4]. Such a hypothesis is also put forward in relation to cholinolytic substances like atropine and its synthetic analogs, which contain a hydroxyl group in the molecule. It is also considered that the hydrogen of the hydroxyl group of the cholinolytic substance participates in a donor-acceptor reaction with some electron donor (atom) which corresponds to the biochemical structure of the organism [5].

Of the synthetic analogs of atropine, β-diethylaminoethyl benzilate (II), mentioned in American pharmacological literature under the symbol WIN 5606, is of considerable interest. Its analog (I), which does not contain a hydroxyl and is known abroad as trasentine and here as spasmolitin, is considerably less active as a cholinolytic.

$$(C_6H_5)_2CHCO-O-CH_2CH_2N(C_2H_5)_2 \quad \text{(I)}$$

$$(C_6H_5)_2C(OH)CO-O-CH_2CH_2N(C_2H_5)_2 \quad \text{(II)}$$

However, among the group of cholinolytic substances containing a hydroxyl there are some that have a low cholinolytic activity. According to the data given by Parkes [6] a particular one of these is 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III), which differs from the active compound (II) in that the CO group in the latter is replaced by a CH_2 group.

$$(C_6H_5)_2C(OH)CH_2-O-CH_2CH_2N(C_2H_5)_2 \quad \text{(III)}$$

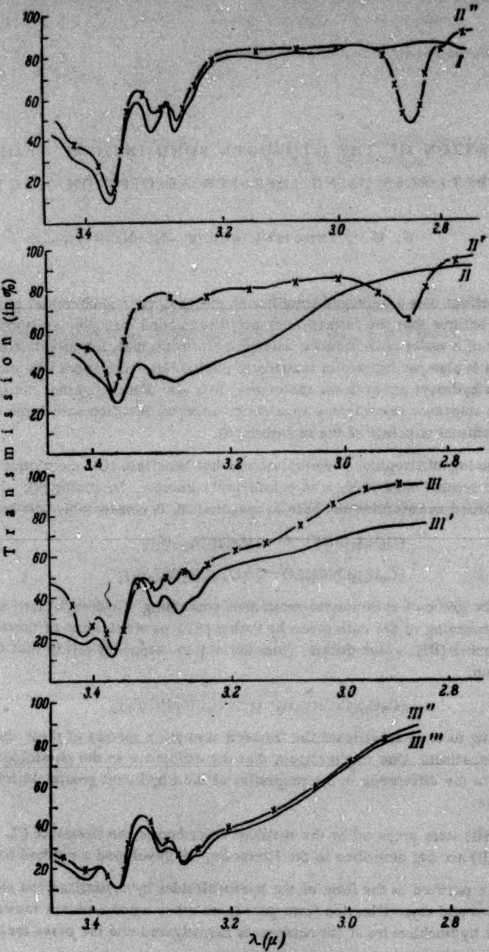
It seemed interesting to us to investigate the infrared absorption spectra of these three compounds, the first being used only for a comparison. One might expect that the difference in the physiological activity of substances (II) and (III) was related to the difference in the properties of their hydroxyl groups, which would also be reflected in their oscillation spectra.

Substances (I) and (II) were prepared by the methods described in the literature [7, 8]. As the synthesis and properties of substance (III) are not described in the literature, we developed a method for its preparation [9].

The substances were purified in the form of the hydrochlorides by crystallization and as the free bases by distillation in high vacuum and crystallization from petroleum ether until constant melting points were obtained. The melting points of the hydrochlorides of the substances investigated and the bases themselves are given below.

Substances (I), (II) and (III) were investigated in the form of free bases. The infrared absorption spectra were plotted on an IKS-146 infrared spectrometer with an LiF prism in the range 2.7-3.5 μ for the pure substances and their solutions in CCl_4. The data obtained are shown in the figure.

Substance (I)(Curve I) has no absorption in the region 3.2-2.8 μ, which agrees with the absence of an OH group in its molecule. In the crystalline state substance (II) has a broad absorption band in the region 3.2-3.0 μ which indicates the presence of a hydrogen bond in it (Curve II). However, when substance (II) is in a molten state (~60°) the broad band in this region disappears and simultaneously a narrow band appears at 2.870 μ which characterizes the oscillation of a free hydroxyl (Curve II'). An analogous picture was observed for a solution of substance (II) in CCl_4, where a narrow band of free hydroxyl appears at 2.855 μ (Curve II"). All this indicates the



Infrared absorption spectra.

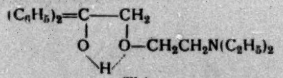
I) $(C_6H_5)_2CHCO-O-CH_2CH_2N(C_2H_5)_2$ solution in CCl_4; (c 0.126 m, d 0.29 mm); II") $(C_6H_5)_2C(OH)CO-O-CH_2CH_2N(C_2H_5)_2$ solution in CCl_4 (c 0.118 m, d 0.29 mm); II and II') $(C_6H_5)_2C(OH)CO-O-$ $-CH_2CH_2N(C_2H_5)_2$, at 20 and 60°, respectively (c 1, d 20μ); III and III') $(C_6H_5)_2C(OH)CH_2-O-CH_2CH_2N(C_2H_5)_2$, at 20 and 100°, respectively (c 1, d 20μ); III" and III"') $(C_6H_5)_2C(OH)CH_2-O-$ $-CH_2CH_2N(C_2H_5)_2$ solutions in CCl_4 (c 0.122 m, d 0.29 mm and c_1 0.00177 m, d_1 20 mm, respectively; $c \cdot d = c_1 \cdot d_1$).

formation of an intermolecular hydrogen bond in substance (II), which is broken when the substance is liquid or dissolved in CCl_4.

Substance	Melting point	
	hydrochloride	Base
(I)	115-116°	Liquid
(II)	177-178	53-55°
(III)	181-182	55.5-56.5

In the crystalline state substance (III) has a broad absorption band at 3.2-3.0 μ, which corresponds to the OH group in the hydrogen bond (Curve III). When the substance is heated above the melting point (100°) no band appears corresponding to the oscillations of free hydroxyls (Curve III').

Curves III″ and III‴ characterize the absorption spectra of solutions of substance (III) at 0.122 and 0.00177 M concentrations in vessels 0.29 and 20 mm thick, respectively (the product of concentration and thickness of solution layer is constant). One can see that absorption in the region of 3.2-3.0 μ does not change with the concentration of substance (III). The invariability of the spectra of substance (III) and the absence of a band at 2.87 μ, which characterizes the oscillation of free hydroxyls, indicate that an intramolecular hydrogen bond exists in substance (III) and remains in the melt and in the solution. This bond probably forms with the participation of the ether oxygen by scheme (IIIa).


(IIIa)

The results obtained seem to indicate that of the three substances investigated only substance (II) should have the tendency to form quite stable intermolecular hydrogen bonds with other suitable substances. Substance (I) cannot have this capacity as it lacks a hydroxyl group, while the hydroxyl group in substance (III) is inactive due to the formation of an intramolecular hydrogen bond. It is noticeable that the results obtained agree with the fact that of the substances investigated only substance (II) has a high cholinolytic activity, while substances (I) and (III) have low and approximately equal activities, which confirms, to a certain degree, the hypothesis of the role of the hydroxyl group in the mechanism of cholinolytic activity of the substances of this series.

SUMMARY

1. We investigated the infrared absorption spectra of three cholinolytic substances: β-diethylaminodiphenylethyl acetate, β-diethylaminoethyl benzilate and 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1.

2. It was concluded from the data obtained that the hydroxyl group in diethyl aminoethyl benzilate was capable of forming an intermolecular hydrogen bond and in 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 an intramolecular hydrogen bond.

3. A hypothesis was put forward on the relation of cholinolytic activity of these compounds to the capacity of their hydroxyl groups to form intermolecular hydrogen bonds.

Received February 8, 1957

All-Soviet Scientific Research
Institute of Sanitation Chemisty

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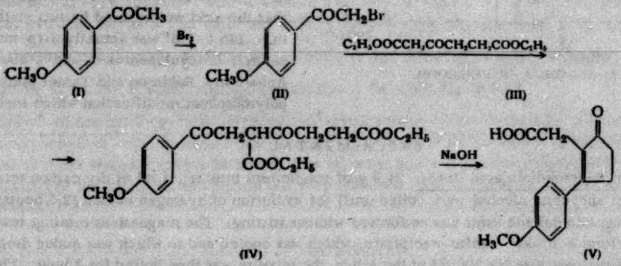
INVESTIGATIONS OF THE SYNTHESIS OF STEROID HORMONE ANALOGS

III. PREPARATION OF 3-(p-METHOXYPHENYL)-Δ^2-CYCLOPENTEN-1-ONE-2-ACETIC ACID

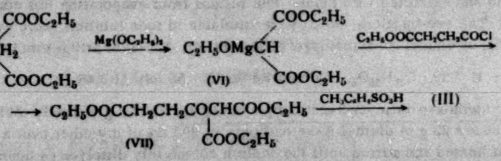
G. S. Grinenko and V. I. Maksimov

3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (V) was the starting material in our work on the complete synthesis of some analogs of steroid hormones. Robinson [1] was the first to prepare this acid from p-methoxyacetophenone and furfurole, in the form of needles with m.p. 133° (after recrystallization from acetone and benzene). Later, Turner [2] used Robinson's method to prepare acid (V) with the same m.p. 132-133°; he prepared its methyl ester with m.p. 87-89°.

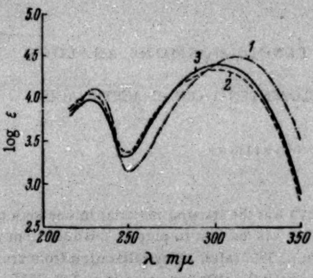
In our work we synthesized acid (V) by another method, based on the process, proposed by Borsche [3] for Δ^2-3-phenylcyclopentenone.


COCH₃
CH₃O
(I)
Br₂
COCH₂Br
CH₃O
(II)
C₂H₅OOCCH₂COCH₂CH₂COOC₂H₅
(III)
COCH₂CHCOCH₂CH₂COOC₂H₅
COOC₂H₅
CH₃O
(IV)
NaOH
O
HOOCCH₂
H₃CO
(V)

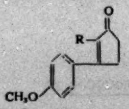
The starting materials were p-methoxy-ω-bromoacetophenone (II) [4] and diethyl β-ketoadipate (III), which was prepared by the method of Riegel and Lilienfeld [5] by acylating the magnesium derivative of diethyl malonate (VI) with the acid chloride of the half ester of succinic acid followed by hydrolysis and decarboxylation of the tricarboxylic ester formed (VII). In contrast to Riegel and Lilienfeld, we prepared ethoxymagnesiomalonic ester (VI) by reacting malonic ester with magnesium alcoholate and not with a suspension of magnesium in alcohol. This decreased the reaction time considerably. We hydrolyzed and decarboxylated the tricarboxylic ester (VII) with p-toluenesulfonic acid and not with naphthalenesulfonic acid.


COOC₂H₅
CH₂
COOC₂H₅
Mg(OC₂H₅)₂
C₂H₅OMgCH
COOC₂H₅
COOC₂H₅
(VI)
C₂H₅OOCCH₂CH₂COCl
C₂H₅OOCCH₂CH₂COCHCOOC₂H₅
COOC₂H₅
(VII)
CH₃C₆H₄SO₃H
(III)

Condensation of diethyl β-ketoadipate (III) with p-methoxy-ω-bromoacetophenone (II) gave a substituted ester of diketoheptanonic acid (IV), which without further purification (as it was converted to the corresponding furancarboxylic ester when distilled) was heated with a 2% solution of sodium hydroxide. Acid (V), obtained by this method in the form of needles, had m.p. 145.5-146° after recrystallization from water, i.e., 12-13° higher than that reported by Robinson and Turner. Recrystallization from acetone and benzene (as performed by these investigators) did not change its melting point.



Ultraviolet absorption spectra of α,β-unsaturated ketones of the type:



1 — R = H, 2 — R = CH_3, 3 — R = CH_2COOH.

We also prepared acid (V) by Robinson's method; it also had melting point 145.5-146° and did not depress the melting point of the acid prepared by our method.

The methyl ester of the acid we prepared had m.p. 88-89°, which agrees with the literature data. By hydrolyzing it we isolated an acid with m.p. 145.5-146°, while when Turner [2] hydrolyzed a methyl ester with the same melting point, he obtained an acid with m.p. 132-133°.

The ultraviolet spectra of acid (I) and its methyl ester are characteristic of α,β-unsaturated ketones, which have a carbonyl group, double bond and aromatic ring conjugated in the molecule [6], and agree with the spectra of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one and 3-(p-methoxyphenyl)-2-methyl-Δ^2-cyclopenten-1-one.

These spectroscopic investigations confirmed that the acid we prepared by two methods with m.p. 145.5-146° was actually 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid. Apparently, Robinson and Turner prepared another polymorphous modification which melted at 133°.

EXPERIMENTAL

Diethyl ester of β-ketoadipic acid III [5]. 24.3 g of magnesium turnings, 4 ml of dry carbon tetrachloride and 157 ml (124 g) of anhydrous alcohol were boiled until the evolution of hydrogen ceased (2.5 hours). The preparation of ethoxymagnesiomalonic ester was performed without stirring. The magnesium turnings reacted with the alcohol vapor to form a friable, white precipitate, which was cooled and to which was added dropwise and with stirring 160 g of malonic ester in 300 ml of dry ether, the mixture was then boiled for 1 hour. Then the alcohol and ether were distilled off from the mixture. The remainder of the alcohol was distilled off with benzene. 185 g of β-carbethoxypropionyl chloride, dissolved in 150 ml of dry ether, was added dropwise with stirring to a solution of the ethoxymagnesiomalonic ester in 300 ml of dry ether and the whole boiled for 2 hours. After being cooled, the reaction mixture was hydrolyzed with 600 ml of 5% sulfuric acid. The ether layer was separated and the aqueous layer extracted with ether. The combined ether extracts were dried. The residue after evaporation of the ether was slowly heated up to 200° in the presence of 14 g of p-toluenesulfonic acid monohydrate until the evolution of carbon dioxide ceased. After being cooled, the reaction mixture was dissolved in ether. The ether solution was washed with a cold, concentrated solution of sodium carbonate and dried. The carbonate solution was acidified with 5% hydrochloric acid and extracted with ether. The residue from evaporating this ether solution was decarboxylated as described above. The two fractions, which were insoluble in soda solution, were evaporated down and distilled. We obtained 125.5 g (58%) of diethyl β-ketoadipate (III) with b.p. 122-126° at 0.5 mm ($n^{20}D$ 1.4555).

Found %: C 55.41; H 7.29. $C_{10}H_{16}O_5$. Calculated %: C 55.54; H 7.46.

Ethyl ester of 2-(p-methoxyphenacyl)-3-ketoadipic acid (IV). To 2.3 g of finely divided metallic sodium in 200 ml of dry ether was added 22 g of diethyl β-ketoadipate in 200 ml of dry ether over a period of 30 minutes. The reaction mixture was heated and stirred until the sodium completely dissolved (4 hours). The solution was cooled, 23 g of p-methoxy-ω-bromoacetophenone [4] in 300 ml of dry ether added and the mixture boiled for 6 hours. The reaction mixture was cooled and water added until the sodium bromide dissolved. The ether layer was separated and the aqueous layer extracted with ether. The combined ether extracts were washed with water and dried with anhydrous sodium sulfate. Evaporation of the ether left 36.2 g (quantitative yield) of ethyl 2-(p-methoxyphenacyl)-3-ketoadipate as a brownish oil, which could be used for intramolecular condensation without purification.

3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (V). 36.2 g of unpurified ethyl 2-(p-methoxyphenacyl)-3-ketoadipate was boiled with 2000 ml of 2% potassium hydroxide with stirring for 1 hour in a stream of nitrogen. During this time the oily layer dissolved completely. The solution was cooled, 100 g of sodium chloride added and the reaction mixture made slightly acid with hydrochloric acid. The oil which separated was extracted with chloroform. The chloroform extract was washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent gave 12.5 g of a brown precipitate. After 2 recrystallizations from 1000 ml of water with charcoal, we obtained 7.3 g (29.7%) of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with m.p. 145.5-146° as long needles with $\lambda_{\max}^{C_2H_5OH}$ 228, 301 mμ, log ε 4.04, 4.33. Recrystallization from acetone and benzene gave 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with constant melting point. The acid was readily soluble in alcohol, acetone, benzene and chloroform and difficultly soluble in ether, benzine and water.

Found %: C 68.19; H 5.76. $C_{14}H_{14}O_4$. Calculated %: C 68.26; H 5.74.

Methyl ester of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid. To a solution of 1 g of the acid (V) and 0.26 g of potassium hydroxide in 20 ml of water was added a solution of 0.7 g of silver nitrate in 10 ml of water and the mixture stirred for 10 minutes. A white precipitate of the silver salt precipitated immediately. This was filtered off and washed on the filter with methyl alcohol and then with ether. The precipitate of the silver salt was placed in a flask and boiled under reflux with 2.6 ml of methyl iodide in 30 ml of ether for 1 hour. The yellow precipitate of silver iodide formed was filtered off. The ether solution was washed with 5% alkali solution, then with water, and dried with anhydrous sodium sulfate. Evaporation of the ether yielded 0.85 g of methyl 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate with m.p. 87-88.5°. After recrystallization from methyl alcohol, the material had m.p. 88-89°. The yield was 80%. $\lambda_{\max}^{C_2H_5OH}$ 228, 301 mμ, log ε 4.03, 4.35. The substance was readily soluble in alcohol, ether, benzene and chloroform and difficultly soluble in benzine.

Found %: C 69.16; H 6.25. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.22.

Hydrolysis of methyl 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate. A solution of 0.3 g of methyl 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate in 10 ml of 2% potassium hydroxide in methyl alcohol was left to stand at room temperature for 24 hours. The reaction mixture was neutralized with acetic acid. The residue from distillation of the methanol in vacuum was recrystallized from 25 ml of water. We obtained the acid (V) with m.p. 145.5-146°.

SUMMARY

1. Starting with p-methoxy-ω-bromoacetophenone and diethyl β-ketoadipate, we synthesized 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with m.p. 145.5-146°.

2. When we prepared this acid by Robinson's method, it had the same m.p. 145.5-146°.

Received November 1, 1957

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INVESTIGATIONS IN THE FIELD OF ANALOGS OF STEROID HORMONES

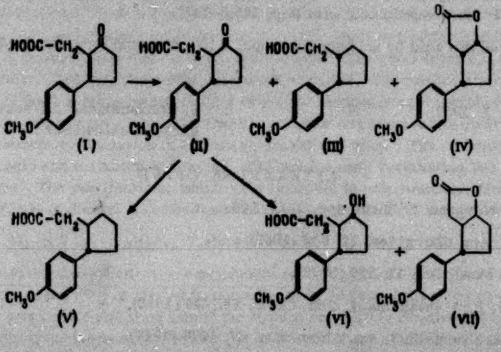
IV. CATALYTIC HYDROGENATION OF 3-(p-METHOXYPHENYL)-Δ^2-CYCLOPENTEN-1-ONE-2-ACETIC ACID

G. S. Grinenko and V. I. Maksimov

During investigations in the field of analogs of steroid hormones, catalytic hydrogenation of the double bond of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (I) gave us trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (II).

The work by Weidlich [1] showed that on reducing a ditertiary double bond of α,β-unsaturated ketones in the presence of a palladium catalyst, a trans-ketone is formed preferentially in an alkaline or neutral medium while a cis-ketone is formed in an acid medium. This observation agrees with the relation between the reaction rate and energy content of the reaction product, established by Zal'kind [2] and Ott [3]. With a rapid rate of hydrogenation (in an acid medium) the isomer mainly formed is that which has a high energy (cis-isomer); as the time of reaction increases (in an alkaline medium) the isomer formed in increasing amount is one with less energy (trans-isomer).

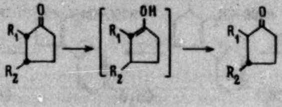
We hydrogenated 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (I) with palladium on calcium carbonate in alkaline (potassium hydroxide, 10% of the acid's weight) and in neutral solutions under atmospheric pressure. The ditertiary double bond was reduced very slowly under these conditions. The application of slight excess pressure (3-5 atm.) considerably increased the hydrogenation rate. In both cases, absorption of hydrogen ceased after the addition of 1.3 moles of hydrogen. The hydrogenation gave a mixture of three substances: trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (II), with m.p. 106.5-107.5° (77%), cis-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (III) with m.p. 73-74° (8.5%) and the lactone of syn-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (IV) with m.p. 67-68° (5.8%).



When hydrogenation was stopped after absorption of 1 mole of hydrogen, in addition to the three substances described above, we isolated the starting keto acid (I). Attempts to further hydrogenate the keto acid (II) isolated under the same conditions (in the presence of a palladium catalyst at 3-5 atm) gave negative results. This indicated that the "perhydrogenation" products (III) and (IV) were formed, not from the saturated keto acid (II), but parallel with it from the unsaturated keto acid (I).

Hoping to obtain another isomer of the saturated keto acid (II), we hydrogenated acid (I) in an acid medium in the presence of palladium on barium sulfate and palladium on charcoal at atmospheric pressure and room temperature. Hydrogen was absorbed very rapidly, without any noticeable slowing down until absorption stopped sharply, after the addition of 3 moles of hydrogen. The only reaction product isolated was cis-acid (III) with m.p. 73-74°. As in the first case, when hydrogenation was stopped after the absorption of 1 mole of hydrogen, a mixture of the starting acid (I) and acid (III) was obtained.

Thus, by hydrogenation we were able to obtain only one stable isomer of keto acid (II), which did not change under conditions favoring enolization. This stable isomer must be a trans-isomer.



To prove the cis-configuration of acid (III), we reduced the carbonyl group in trans-keto acid (II) using the Clemmensen method as modified by Martin [4] for keto acids. This gave trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (V) with m.p. 55-56°, as the asymmetric centers are not involved in the reduction of the keto group.

To prove the syn-cis-configuration of lactone (IV), we reduced the carbonyl group in trans-keto acid (II) with sodium borohydride. The reaction proceeded sterically to form 73.6% anti-trans-hydroxy acid (VI) with m.p. 86-87° and 24% anti-cis-hydroxy acid, isolated as the lactone (VII) with m.p. 141-142°. Hydroxy acid (VI), obtained from trans-keto acid (II), did not lactonize even after prolonged treatment with hydrochloric acid solution. This proves its anti-trans-configuration according to the rule given by Alder and Stein [5]. On the contrary, lactones(VII) and (IV), which are diastereoisomers, could not be opened either by careful acidification of the sodium salt to a neutral reaction (a hydroxy acid could have been formed) or by treatment of the silver salt of the hydroxy acid with methyl iodide (here one might expect the formation of the corresponding methyl ester). Such stability of the lactone ring is due to the absence of strain in cis-biscyclooctane-(0,3,3).

Thus, we can accept that lactone (IV) with m.p. 67-68° has a syn-cis- and lactone (VII) an anti-cis-configuration.

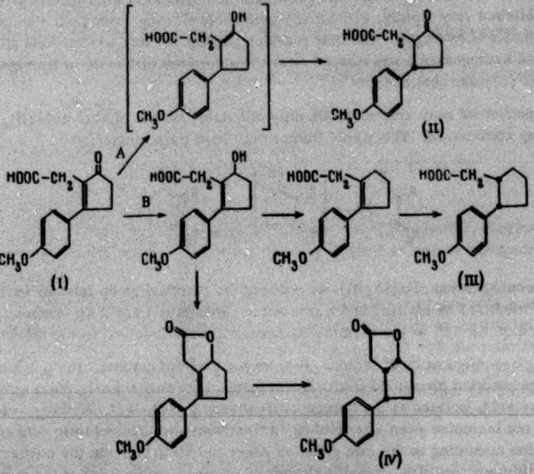
The results of hydrogenating acid (I) agree with the mechanism, proposed by Weidlich [1] and Teilacker and Drössler [6], for the catalytic hydrogenation of α,β-unsaturated ketones, as shown by the following scheme.

$$\begin{tikzcd}
R_2C{=}CHCOR \arrow[r, "A"] \arrow[d, "B"] & {[R_2CHCH{=}C(OH)R]} \arrow[r] & R_2CHCH_2COR \\
R_2C{=}CHCH(OH)R \arrow[r] & R_2C{=}CHCH_2R \arrow[r] & R_2CHCH_2CH_2R
\end{tikzcd}$$

Hydrogen may be added either at the C=C (A direction) or C=O (B direction) double bond. In the first case, a saturated ketone is produced which under conditions favoring enolization, is converted into a stable form of ketone (trans- or cis-). A saturated ketone may also be formed as a result of 1,4-addition of hydrogen followed by the conversion of the enol to a stable form of ketone. In the second case, an unsaturated alcohol of an allyl type is formed, which is very readily reduced further under the experimental conditions, to form a saturated hydrocarbon. The authors were unable to isolate the intermediate products. Direction B assumes 1,2-addition of hydrogen, which is analogous to the hydrogenation of an isolated multiple bond [7] and therefore, gives, as a rule, a cis-hydrocarbon.

In our case, when acid (I) was hydrogenated in an alkaline and neutral medium, trans-keto acid (II) was formed by scheme A and cis-acid (III) by scheme B. The syn-cis-hydroxy acid lactone (IV) could have been formed only from an intermediate, unsaturated lactone, whose double bond was activated by the aromatic ring and therefore readily reduced under the experimental conditions. In the case of hydrogenation in an acid medium, the reaction proceeded only by direction B; therefore the saturated ketone could not be isolated.

Using the reduction of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid as an example, the mechanism of the reduction of α,β-unsaturated ketones may be represented by the following scheme.



EXPERIMENTAL

Catalytic Hydrogenation of 3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic Acid

1. Hydrogenation in neutral medium. 31 g of the acid (I) was hydrogenated in an autoclave in the presence of 10 g of 5% palladium on calcium carbonate as catalyst in 210 ml of methyl alcohol with 3 atmospheres of hydrogen until the absorption of hydrogen ceased (1.3 moles). The catalyst was then filtered off and washed with methanol. The methyl alcohol was distilled off in vacuum to leave a colorless, immobile oil, consisting of three substances, which were separated in two ways.

a) First method. The oil was dissolved in benzene. The acids were extracted from the benzene solution by shaking the latter with 5-6 portions of 5% sodium carbonate solution (50 ml each). Careful acidification of each portion of the soda solution gave a precipitate of acid. The first three fractions contained trans-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid as right prisms. The precipitate was filtered off and washed with water on the filter to a neutral reaction to litmus. We obtained 23.9 g of acid (II) with m.p. 104-105°; after recrystallization from 50% alcohol the substance had m.p. 106.5-107.5°. The yield was 77%. The acid (II) was very readily soluble in almost all organic solvents, difficultly soluble in benzine and slightly more soluble in ether.

Found %: C 67.73; H 6.55. $C_{14}H_{16}O_4$. Calculated %: C 67.72; H 6.49.

The fifth and sixth fractions contained 2.5 g of the acid (III) in the form of fine needles with m.p. 73-74°. The yield was 8.5%. The substance was readily soluble in almost all organic solvents, apart from benzine.

Found %: C 71.72; H 7.68. $C_{14}H_{18}O_3$. Calculated %: C 71.77; H 7.74.

The fourth fraction contained 3.2 g of a mixture of the two acids (II) and (III) which had m.p. 65-69°; acid (II) was separated from this mixture by conversion to the semicarbazone.

Evaporation of the original benzene solution yielded 1.7 g (5.8%) of the syn-cis-lactone (IV) in the form of platelets, agglomerated as nodules, with m.p. 66-67°. After recrystallization from a 5-fold amount of an ether – benzene mixture (1 : 4), the substance had m.p. 67-68°. The lactone was readily soluble in alcohol, benzene and chloroform and difficultly soluble in ether and benzine; it dissolved in an aqueous solution of alkali and immediately lactonized on acidification.

Found %: C 72.30; H 6.97. $C_{14}H_{16}O_3$. Calculated %: C 72.39; H 6.94.

b) Second method. The oil was dissolved in 100 ml of ether. After cooling, the solution gradually deposited a precipitate of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (II), which was filtered off and washed with a small amount of ether on the filter. We obtained 22.1 g of the acid with m.p. 106.5-107.5° (70.9%). The ether mother liquors, which contained a mixture of the trans-keto acid (II), the cis-acid (III) and the syn-cis--lactone (IV) was worked up by the method described above.

The methyl ester of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid was prepared by reacting the silver salt of the acid with methyl iodide and formed colorless prisms with m.p. 39.6-41°, which were readily soluble in all organic solvents, except for benzine.

Found %: C 68.99; H 6.93. $C_{15}H_{18}O_4$. Calculated %: C 68.68; H 6.92.

The semicarbazone of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid formed colorless crystals with m.p. 184° (with decomp.) after recrystallization form alcohol.

Found %: N 13.83. $C_{15}H_{19}O_4N_3$. Calculated %: N 13.76.

To decompose the semicarbazone of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid, a mixture of 3.35 g of the semicarbazone, 2.2 ml of 38% formaldehyde solution and 15 ml of 80% acetic acid was slowly heated to 70°. The semicarbazone dissolved completely. The reaction mixture was kept at 70° for 1 hour. After cooling, the reaction mixture was poured into water. The precipitated acid was extracted with benzene. The benzene extract was washed with water until neutral to litmus and dried with anhydrous sodium sulfate. The benzene was distilled off in vacuum to yield 2.7 g (quantitative yield) of acid (II) with m.p. 102-104°. After recrystallization from 50% alcohol, the substance had m.p. 106.5-107.5°.

2. Hydrogenation in acid medium. a) Hydrogenation with Pd/ $BaSO_4$. To 0.5 g of previously reduced 2% palladium on barium sulfate in 20 ml of chemically pure methyl alcohol was added 1 g of acid (I) and 2 ml of 6 N hydrogen chloride in methyl alcohol. The hydrogenation was performed at atmospheric pressure and room temperature. The absorption of hydrogen ceased after the absorption of 3 moles (30 minutes). The catalyst was filtered off and washed with methyl alcohol. After distilling off the solvent we obtained a quantitative yield of acid (III) with m.p. 73-74°, which did not depress the melting point of the acid obtained after hydrogenation in neutral or alkaline solutions.

b) Hydrogenation with Pd on charcoal. 2 g of acid (I) was hydrogenated in the presence of 1 g of 5% palladium chloride on charcoal in 30 ml of methyl alcohol at room temperature and normal pressure. The hydrogen chloride liberated during the reduction of the catalyst provided the acid medium. The absorption of hydrogen stopped after the addition of 3 moles. The isolation was as in the previous experiment. We obtained a quantitative yield of acid (III) with m.p. 73-74°.

c) Hydrogenation up to the addition of 1 mole of hydrogen. 1 g of acid (I) was hydrogenated in the presence of 0.5 g of 2% palladium on barium sulfate in 20 ml of methyl alcohol in an acid medium. The absorption of hydrogen was stopped when 1.05 moles had been absorbed. The catalyst was filtered off. The residue from evaporation of the methyl alcohol was treated with 10 ml of ether. The ether-insoluble precipitate was filtered off to give 0.65 g of the starting acid (I) with m.p. 145-146°. After evaporation of the solvent, the ether solution yielded 0.25 g of acid (III) with m.p. 73-74° (after recrystallization from a mixture of benzine and ether).

Trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (V). The acid (V) was obtained by a Clemmensen reduction of acid (II). To prepare amalgamated zinc, a mixture of 20 g of zinc turnings, 2 g of mercuric chloride, 30 ml of water and 1 ml of concentrated hydrochloric acid was shaken for 5 minutes. The aqueous solution was decanted, the amalgamated zinc treated with 15 ml of water, 30 ml of concentrated hydrochloric acid and 20 ml of toluene and 10 g of acid (II) added. The reaction mixture was boiled vigorously for 30 hours. During this time 10 ml portions of concentrated hydrochloric acid were added every 6 hours. The reaction mixture was cooled, the toluene layer separated and the aqueous layer extracted with benzene. The toluene–benzene extract was washed with water until neutral to litmus and dried with anhydrous sodium sulfate. Distilling off the solvent left a colorless oil, which quickly crystallized in the form of needles. After recrystallization from petroleum ether, we obtained 7.1 g (75%) of acid (V) with m.p. 54.5-55.5° – the diastereoisomer of the acid (III), obtained after catalytic hydrogenation of acid (II). The substance was readily soluble in almost all organic solvents.

Found %: C 72.05; H 7.63. $C_{14}H_{18}O_3$. Calculated %: C 71.77; H 7.74.

Reduction of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-acetic acid with sodium borohydride. To a solution of the sodium salt, prepared from 12.4 g of acid (II) and 2.18 g of 92% sodium hydroxide in 70 ml of water, was added a solution of 3 g of sodium borohydride in 50 ml of water. The reaction mixture was allowed to stand for 1 hour at room temperature and then the excess sodium borohydride was decomposed with several drops of acetic acid. Then the reaction mixture was made weakly acid to litmus with dilute hydrochloric acid. The precipitate formed was extracted with chloroform. The anti-trans-hydroxy acid (VI) was washed out of the chloroform extract by shaking the latter with 5% soda solution. After acidification of the combined soda solutions, the precipitate formed was filtered off, washed with water and dried. We obtained 9.5 g (76%) of acid (VI) with m.p. 84.5-86°; recrystallization from 20 ml of benzene yielded 9.19 g (73.6%) of acid (VI) with m.p. 86-87°. The substance was readily soluble in alcohol, acetone, ether, benzene and chloroform and difficultly soluble in benzine.

Found %: C 67.22; H 7.26. $C_{14}H_{18}O_4$. Calculated %: C 67.18; H 7.25.

Evaporation of the ether solution yielded 2.8 g (24%) of lactone (VII) with m.p. 141-142° (after recrystallization from alcohol). The lactone anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid was the diastereoisomer of lactone (IV) with m.p. 67-68°, obtained after catalytic hydrogenation. The lactone (VII) was difficultly soluble in ether, benzene and benzine and slightly more soluble in chloroform and alcohol.

Found %: C 72.63; H 7.03. $C_{14}H_{16}O_3$. Calculated %: C 72.40; H 6.94.

Anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid. To. 1.25 g of the anti-trans-hydroxy acid (VI), placed in a Claisen flask, was added 1.25 ml of acetyl chloride. The reaction mixture gave off heat. As soon as the precipitate dissolved (1-2 minutes), the excess acetyl chloride was distilled off in vacuum. The oily residue crystallized after standing for several hours. Two recrystallizations from a mixture of benzene and benzine yielded 1.05 g of anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid with m.p. 91.5-92°. The yield was 72%. The substance was readily soluble in the usual organic solvents with the exception of benzine.

Found %: C 65.99; H 6.91. $C_{16}H_{20}O_5$. Calculated %: C 65.73; H 6.90.

Attempted preparation of the methyl ester of syn-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid. 1.67 g of the syn-cis-lactone of the hydroxy acid (IV) was boiled with a solution of 0.49 g of 87% potassium hydroxide in 30 ml of water for 0.5 hours. During this time the lactone dissolved completely. The solution was cooled and to it was added 30 ml of methyl alcohol and a solution of 1.24 g of silver nitrate in 8.5 ml of water. A white precipitate of the silver salt formed immediately. After 10 minutes mixing, 9.4 g of methyl iodide was added. After a further 15 minutes mixing, the yellow precipitate of silver iodide formed was filtered off. The mother liquor was evaporated down to yield an oily substance, which was extracted with ether. The ether extract was washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent yielded 1.6 g of syn-cis-lactone (IV) with m.p. 66-68°, which did not depress the melting point of the original lactone.

Attempted preparation of the methyl ester of anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid. Under the reaction conditions described above, the trans-lactone of 3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (VII) also gave a quantitative yield of the starting lactone with m.p. 141-142°.

SUMMARY

1. The catalytic hydrogenation of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid in the presence of a palladium catalyst was studied in an acid and in alkaline and neutral media. It was established that hydrogenation in an alkaline and in a neutral medium gave 3 substances: trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid, the lactone of syn-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid and cis-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid, while hydrogenation in an acid medium gave the latter exclusively.

2. It was shown that reduction of the carbonyl group of trans-3-(p-methoxyphenyl)-cyclopentan-2-one-2-acetic acid with sodium borohydride proceeded sterically to form 73% of anti-trans-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid; the other epimer was isolated in the form of the lactone of anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (24%).

3. The isolation of the intermediate alcohol (the hydroxy acid in the form of its lactone) confirmed the mechanism proposed earlier for the catalytic hydrogenation of α,β-unsaturated ketones.

Received November 1, 1957

All-Soviet Institute of
Chemical Pharmaceutical
Research

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RESIN ACIDS

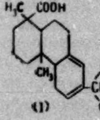
I. THE NATURE OF α-SAPINIC ACID

I. I. Bardyshev and V. V. Kokhomskaia

α-Sapinic acid was first isolated by Dupont and Dubourg [1] from the soft resin of Pinus maritima Mill. It was later also isolated from the soft resin of native, coniferous Pinus silvestris L. [2, 3] and Picea excelsa Link[4]. According to these investigations, α-sapinic acid constitutes about 55% of the total of resin acids from soft resin, which are a large-scale product of the wood pulp chemical industry of the USSR. V. N. Krestinskii et al.[5] and V. M. Akulovich [6] devoted their investigations to determining the structural formula of α-sapinic acid. D. V. Tishchenko et al. [7] studied the autooxidation of α-sapinic acid and the structure of the higher autooxidation product of this acid. As can be seen from these papers, the majority of the Soviet investigators consider α-sapinic acid to be an individual resin acid. B. A. Arbuzov [8] was the only one who had some doubt on the individuality of α-sapinic acid.

In studying the composition of resin acids in soft resins of various native conifers [9, 10], we could not ignore the problem of the individuality of α-sapinic acid.

The present investigation showed that the so-called α-sapinic acid is not a single acid but is a complex mixture consisting of levopimaric (I), palustric (II), neoabietic (III), abietic (IV) and dextropimaric (V) resin acids. It should be noted that the structure of palustric acid (II) has not yet been established definitely [11].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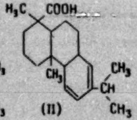
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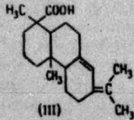
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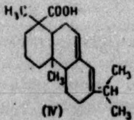
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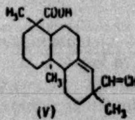
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EXPERIMENTAL

α-Sapinic acid was isolated from the resin of Pinus silvestris by the method of Krestinskii et al. [2] and had m.p. 146-148° and $[\alpha]_D$ −64.6°. Its ultraviolet absorption spectrum is shown in Fig. 1 (Curve 1). According to its properties, the α-sapinic acid we isolated was identical to the α-sapinic acid obtained by Krestinskii et al.

Isolation of levopimaric acid. To a solution of 150 g of α-sapinic acid in 350 ml of ether was added 100 g of a saturated ether solution of bornylamine in small portions. The reaction mixture was left for 12 hours at room temperature then the salt formed was filtered off and washed many times on the filter with ether. We obtained 151 g of the bornylamine salt (salt A) with m.p. 135-149° and $[\alpha]_D$ −59.6°. The UV-spectrum of salt A is shown in Fig. 1 (Curve 2). The first crystallization of the salt from alcohol gave 50 g of a crystalline product with m.p. 165-175° and $[\alpha]_D$ −165.0°, and after three recrystallizations we obtained 5 g of the salt of bornylamine and levopimaric acid with m.p. 185-187° and $[\alpha]_D$ −191.2°. Its UV-spectrum is shown in Fig. 1 (Curve 3). To isolate free levopimaric acid, 2 g of the salt obtained was decomposed with an aqueous solution of boric acid and the mixture extracted with ether. The ether layer was separated, washed with water and dried with magnesium sulfate. The residue from evaporation of the ether was recrystallized three times from alcohol to yield 0.06 g of levopimaric acid (Table and Fig. 1, Curve 4).

Isolation of palustric acid. The ether mother liquor, obtained after separation of the bornylamine salt A, was treated with an aqueous solution of boric acid. The acid remaining after evaporation of the ether was dissolved in acetone and 13.5 g of diethylamine was added to the solution. The salt obtained was recrystallized from acetone. Five recrystallizations yielded 1.7 g of the salt of diethylamine and palustric acid with m.p. 133.5-138.5° and $[\alpha]_D$ + 50.7°. Its UV-spectrum is shown in Fig. 2 (Curve 2). Further recrystallization of the salt did not change its specific rotation or specific absorption coefficient. As a result of decomposing this salt (1.55 g) with boric acid and recrystallizing the products obtained 3 times from alcohol, we isolated 0.12 g of palustric acid (Table and Fig. 2, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

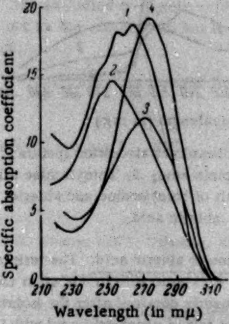

Fig. 1. Ultraviolet absorption spectra. 1) α-sapinic acid; 2) bornylamine salt A; 3) salt of bornylamine and levopimaric acid; 4) levopimaric acid.

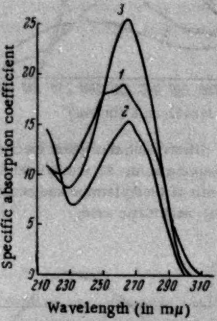

Fig. 2. Ultraviolet absorption spectra. 1) α-sapinic acid; 2) salt of diethylamine and palustric acid; 3) palustric acid.

Isolation of neoabietic acid. The mother solution, remaining after the isolation of the diethylamine salt of palustric acid, was treated with boric acid to regenerate resin acids. The acids obtained were converted to the bornylamine salts and recrystallization of these from ether gave a bornylamine salt with m.p. 120-138° and $[\alpha]_D$ −15.3°. The latter was combined with the bornylamine salt obtained from the mother solution left after separation of levopimaric acid. The resin acids (47 g), obtained by decomposing the salt fractions described above with boric acid had $[\alpha]_D$ −15.0°. To remove levopimaric acid under conditions excluding isomerization, 50 ml of petroleum ether distilled over sodium was added to the mixture of acids obtained, followed by 10 g of twice-distilled maleic anhydride in 10 ml of dry acetone. At this the temperature rose from 23 to 32°. The reaction mixture was left at room temperature for 12 hours and then it was poured into 433 ml of 3% sodium hydroxide solution. The petroleum ether was separated and the solution diluted to 2.6 liters with water and acidified to pH ≈ 6 with dry boric acid. The acids which had not reacted with maleic anhydride were precipitated with sodium sulfate, filtered off, washed several times with distilled water on the filter and dissolved in ether. The ether layer was separated and dried with magnesium sulfate. The mixture of resin acids obtained had $[\alpha]_D$ + 52.3°. To the ether solution of this mixture of acids was added 6.5 g of ethanolamine. The product formed was filtered off and washed with ether on the filter. We obtained 27 g of an ethanolamine salt with m.p. 113-134° and $[\alpha]_D$ + 49.7° and recrystallization of this from ethyl acetate gave 13 g of an ethanolamine salt with $[\alpha]_D$ + 61.5°. The latter was decomposed with an aqueous solution of boric acid. The residue from evaporation of the ether was dissolved in acetone and 3.5 ml of diethylamine was added to the acetone solution. The salt formed was filtered off and washed with acetone on the filter. We obtained 10 g of a diethylamine salt (salt B) with m.p. 107-116.5° and $[\alpha]_D$ + 67.1° (The UV-spectrum is shown in Fig. 3, Curve 2). Two recrystallizations of this product from acetone yielded the salt of neoabietic acid and diethylamine with m.p. 152-155° and $[\alpha]_D$ + 120.6°. (The UV-spectrum is shown in Fig. 3, Curve 3). 0.55 g of the neoabietic acid salt was decomposed with an aqueous solution of boric acid. The residue from evaporation of the ether was recrystallized twice from alcohol; we thus isolated 0.07 g of neoabietic acid (Table and Fig. 3, Curve 4).

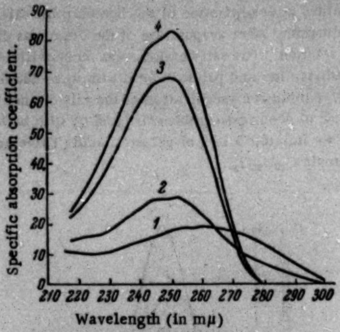

Fig. 3. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) diethylamine salt B; 3) salt of diethylamine and neoabietic acid; 4) neoabietic acid.

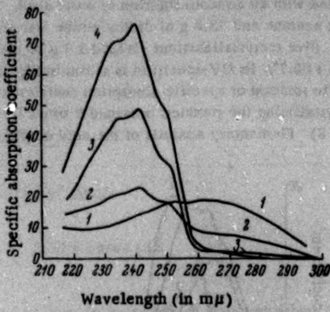

Fig. 4. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) bornylamine salt C; 3) salt of bornylamine and abietic acid; 4) abietic acid.

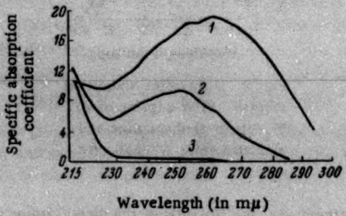

Fig. 5. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) ethanolamine salt D; 3) salt of ethanolamine and dextropimaric acid.

Isolation of abietic acid. The resin acids were regenerated with boric acid by the usual method from the mother liquors obtained after the isolation of the ethanolamine salt of neoabietic acid with $[\alpha]_D$ + 49.7 and +61.5°. To an alcohol solution of the acids was added 10 g of a saturated ether solution of bornylamine. The product formed was filtered off and washed with alcohol on the filter. We obtained 4.7 g of a bornylamine salt (salt C) with m.p. 131.5-137.5° and $[\alpha]_D$ +16.6°. (The UV-spectrum is shown in Fig. 4, curve 2). Four recrystallizations of this fraction from alcohol yielded 0.25 g of the salt of bornylamine and abietic acid with m.p. 155-156.5° and $[\alpha]_D$ −47.5° (The UV-spectrum is shown in Fig. 4, Curve 3). 0.2 g of the abietic acid salt was decomposed with boric acid. The residue from evaporation of the ether was recrystallized from alcohol; this yielded 0.045 g of abietic acid (Table and Fig. 4, Curve 4).

Physical Properties of Resin Acids Isolated from α-Sapinic Acid (Upper Series of Figures) and Comparison of them with Literature Data

Name of acid	Melting point	$[\alpha]_D$ of alcohol solution	Specific absorption coefficient	Position of absorption maximum (in mμ)
Levopimaric acid	150—152°	—277.0°	19.3	272.5
According to literature data [12,13]	150—152	—275.0	19.2	272.0
Neoabietic acid	169—170.5	+162.9	81.4	250—251
According to literature data [10]	177.5—179	+175.0	80.5	250—251
Abietic acid	170—172	—105.6	75.6	241
According to literature data [9]	174—175	—116.0	85.0	241
Palustric acid	167.5—169.5	+ 71.4	25.5	266
According to literature data [11]	162—167	+ 71.8	31.0	265—266

Isolation of ethanolamine salt of dextropimaric acid. From the mother solution, obtained after the isolation of the bornylamine salt with m.p. 120-138° and $[\alpha]_D$ −15.3° (see section on neoabietic acid), we regenerated the resin acids and then converted the latter into the ethanolamine salt. Recrystallization of this salt from ethyl acetate gave a second fraction of crystals (0.2 g) with m.p. 146.5-154.5° (salt D; Fig. 5, Curve 2). After 3 recrystallizations of this fraction from ethyl acetate, we isolated 0.02 g of the ethanolamine salt of dextropimaric acid with m.p. 164-166° and $[\alpha]_D$ +49.5° (The UV-spectrum is shown in Fig. 5, Curve 3). The ethanolamine salt, prepared from a sample of dextropimaric acid with m.p. 218-219°, melted at 167-169°.

SUMMARY

1. The so-called α-sapinic acid, isolated from the soft resin of Pinus silvestris by the method of Krestinskii et al., is not an individual acid, but is a mixture of levopimaric, palustric, neoabietic, abietic and dextropimaric resin acids.

2. Palustric acid was isolated from the soft resins of Pinus silvestris for the first time.

Received January 14, 1957

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RESIN ACIDS

II. THE NATURE OF β-SAPINIC ACID

I. I. Bardyshev and L. I. Ukhova

β-Sapinic acid was first isolated from the soft resin of Pinus maritima Mill. According to Dupont [1], this soft resin consists of the following acids: α-sapinic (49%), β-sapinic (21%), levopimaric (21%) and dextropimaric (9%). Krestinskii et al. [2] found that the soft resin of Pinus silvestris L. contained β-sapinic acid (5%), in addition to α-sapinic (55%), levopimaric (30%) and dextropimaric (10%) acids.

However, the structural formula of β-sapinic acid was not established. Furthermore, the problem of whether this acid is an individual acid has not yet been solved [3].

The present investigation showed that β-sapinic acid, obtained by the method of Krestinskii, is not an individual acid, but consists of levopimaric (about 60%), neoabietic and abietic acids. It is also possible that other resin acids are included in small amounts in the composition of β-sapinic acid.

EXPERIMENTAL

β-Sapinic acid. We isolated this acid from the soft resin of Pinus silvestris by the method of V. N. Krestinskii [2] and it had m.p. 139-143° and $[\alpha]_D$ −94.5°. Its UV-spectrum is shown in Fig. 1, Curve 1. In all, 40 kg of soft resin was processed; from it we obtained 24 kg of mixed resin acids, from which we isolated 200 g of β-sapinic acid.

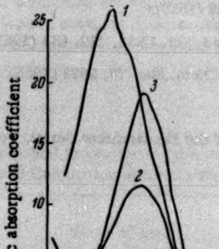

Fig. 1. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) bornylamine salt of levopimaric acid; 3) levopimaric acid.

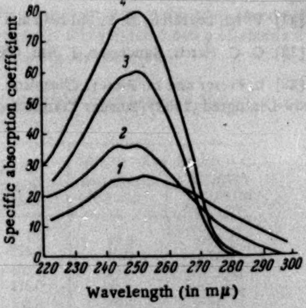

Fig. 2. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) resin acids, which do not react with maleic anhydride; 3) diethylamine salt of neoabietic acid; 4) neoabietic acid.

Isolation of levopimaric acid. To 180 g of a solution of β-sapinic acid in ether was added 90 g of bornylamine as an ether solution. The product was washed with ether and dried to yield 248 g of the bornylamine salt of β-sapinic acid with m.p. 128-152° and $[\alpha]_D$ −79.1°. 40 g of the salt was recrystallized 3 times from alcohol; as a result we obtained a salt with m.p. 185-187° and $[\alpha]_D$ −179° (its UV-spectrum is shown in Fig. 1, Curve 2). The salt was decomposed with an aqueous solution of boric acid and the levopimaric acid obtained as a result of this was recrystallized twice from alcohol, when it had the constants: m.p. 149.5-151°, $[\alpha]_D$ −276°, specific absorption coefficient 19.0 at 272 mμ (Fig. 1, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

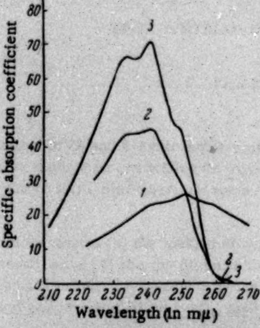

Fig. 3. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) bornylamine salt of abietic acid; 3) abietic acid.

Isolation of neoabietic acid. β-Sapinic acid (140 g) was treated with maleic anhydride under conditions excluding isomerization [4]. As a result of the treatment we obtained 42.4 g of resin acids which did not react with maleic anhydride and had $[\alpha]_D$ +59° (the UV-spectrum is shown in Fig. 2, Curve 2). To 40 g of an acetone solution of these resin acids was added 10 g of diethylamine dissolved in acetone. The salt formed was washed with acetone and dried. We obtained 33.5 g of crystals with $[\alpha]_D$ +56°, which were recrystallized 4 times from acetone. During this the specific rotation of the salt first increased and then remained constant ($[\alpha]_D$ + 98.7°, +111.5°, +109.8°, + 109.8°). 3.35 g of the diethylamine salt (m.p. 153-157° and $[\alpha]_D$ +109.8°) was decomposed with an aqueous solution of boric acid by the usual method. After two recrystallizations from alcohol, the neoabietic acid obtained in this way had m.p. 179-180.6°, $[\alpha]_D$ +171.2° and a specific absorption coefficient of 79.3 at 250 mμ (Fig. 2, Curve 4). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

Data on x-ray analysis, carried out in the Laboratory of the Physical Chemistry Institute of the Academy of Sciences of the Byelorussian SSR, showed that neoabietic acid has a primitive elementary cell of the rhombic syngony with the axes: a 6.11 A, b13.15 and c 21.39 A.

Isolation of abietic acid. The mother liquors of the diethylamine salts, obtained after the isolation of neoabietic acid, were combined and evaporated to dryness and the salt decomposed with boric acid. To the resin acids was added bornylamine and as a result we obtained 28 g of a salt. After recrystallizing it from alcohol, we isolated 5 g of crystals with m.p. 138-144°. Four recrystallizations from alcohol yielded bornylamine abietate with m.p. 158.5-160.5° and $[\alpha]_D$ −38.6° (the UV-spectrum is shown in Fig. 3, Curve 2). 0.24 g of bornylamine abietate was decomposed with boric acid in the usual way. After two recrystallizations from alcohol, the abietic acid had m.p. 171.5-173°, $[\alpha]_D$ −93°, specific absorption coefficient 70.7 at 241 mμ (Fig. 3, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

SUMMARY

β-Sapinic acid, isolated from the soft resin of Pinus silvestris L. by Krestinskii's method, is not an individual resin acid but is a mixture of levopimaric, abietic and neoabietic acids and, possibly, of small amounts of other resin acids.

Received January 14, 1957

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INVESTIGATIONS IN THE FIELD OF QUINOLINE DERIVATIVES

XVII. SYNTHESIS OF SOME 6- AND 8-ALKOXYQUINOLINES

B. I. Ardashev and V. I. Minkin

The ethers of 6- and 8-hydroxyquinolines are used for preparing cyanine dyes and medicines. The absence of an effective method for controlling the vigorous course of the Skraup reaction [1] and the low yields of 8-alkoxyquinolines, due to steric hindrance, are some of the disadvantages of the existing methods for synthesizing these ethers.

For various reasons [2] the method of adding a double amount of H_2SO_4 to the reaction mixture [3], the use of Kone's modification [4] and the direct introduction of acrolein into the reaction [5] cannot be recommended. We did not obtain satisfactory results in trying to obtain alkoxyquinolines directly from nitro compounds (in analogy with Das' work) or by using dilute H_2SO_4, used previously in some works [6-9].

A good yield with a smooth reaction course was achieved by gradually adding (over a period of 10-20 minutes) a mixture of amine, sulfuric acid and glycerin to the oxidizing agent, heated to a temperature above that of the reaction. Walter [10] was the first to propose this method; Manske [11] recently recommended it. Our modification is preferable to the alkylation of 8-hydroxyquinoline [12, 13] or the synthesis using arsenic acid by Knueppel's method [14, 15].

EXPERIMENTAL

The syntheses were performed in a three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a thermometer.

6-Methoxyquinoline. 11 g of p-nitroanisole was heated to 170° and over a period of 30-60 minutes a mixture of 13 g of p-anisidine, 12.5 ml of sulfuric acid (s.g. 1.82and 60 g of glycerin, kept at the temperature of a water bath, was introduced through the condenser. Toward the end of the addition, the temperature of the gently boiling mixture was 150° and after a further 5-5.5 hours, 134°. The remainder of the p-nitroanisole was removed by steam distillation, the mixture made alkaline and then the 6-methoxyquinoline distilled off in steam (p-anisidine does not distill over at this point [16]). We isolated 10.8 g (64%) of 6-methoxyquinoline. The b.p. was 127-130° (at 5 mm). The picrate had m.p. 209°; the iodomethylate had m.p. 236°.

8-Methoxyquinoline. We used 10 g of o-anisidine, 29 g of glycerin, 12 ml of sulfuric acid and 12 g of o-nitroanisole. The mixture was heated for 3.5 hours. The temperature at the beginning of the reaction was 200° and at the end, 133°. We obtained 4.9 g (38%) of 8-methoxyquinoline with b.p. 155° (13 mm). The picrate had m.p. 162.5°; the iodomethylate had m.p. 161°.

8-Ethoxyquinoline. To 7 g of o-nitrophenol and 1 g of $FeSO_4 \cdot 7H_2O$, at 150° was added a heated mixture of 13.7 g of o-phenetedine, 18 ml of sulfuric acid (s.g. 1.82) and 30g of glycerin. At the end of the addition (after approximately 18 minutes) the temperature was 150° and after a further 2 hours, 137°. The whole of the o-nitrophenol reacted and none distilled off with steam. The mixture was made alkaline and extracted twice with large amounts of benzene for better separation of the layers. The tar was filtered off from the benzene extract, which was washed, the benzene distilled off, the residue dissolved in ether and the ether extract filtered free from tar and treated twice with phthalic anhydride (portions of 10 and 6 g) to separate the tertiary amine [17]. The phthalaminic acid formed was extracted with 10% sodium hydroxide solution. Evaporation of the ether yielded 6.8 g

(39.7%) of 8-ethoxyquinoline. The b.p. was 200° (29 mm). The picrate had m.p. 180°; the iodomethylate had m.p. 199°.

6-Ethoxyquinoline. 10 g of p-phenetedine, 39 g of glycerin, 9 ml of sulfuric acid and 7.5 g of o-nitrophenol were used. The mixture was heated for 5.5 hours. The temperature at the beginning of the reaction was 160° and at the end, 137°. We obtained 6.3 g (50%) of 6-ethoxyquinoline with b.p. 289°. The picrate had m.p. 194°; the iodomethylate had m.p. 196°.

SUMMARY

A method for synthesizing the ethers of 6- and 8-hydroxyquinolines was developed from Walter's modification, with greater yields than those obtained by known methods.

Received January 31, 1957

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INVESTIGATION OF THE CRYSTALLINE [illegible] IN THE PRODUCTION OF [illegible]

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products of anabasine sulfate production, of which aphyllinic acid sulfate is one. It is possible that such a method for producing aphylline may be of practical value, as according to data in the literature [4], aphylline is a pharmacologically active substance (anesthesia).

In investigating the substance obtained during the melting of aphyllinic acid hydrochloride, we isolated a small amount of a crystalline, optically active substance that was isomeric with aphylline. We obtained the same substance from the reaction mass, obtained by heating aphylline hydrochloride to 265°. We may surmise that this substance, which we temporarily denoted as "substance B", may be one of the eight possible stereoisomers of sparteine with an oxo group in the inner ring, the more so as some of the properties of this substance are quite similar to those of oxo-β-isosparteine [5]. The study of this substance is being continued.

EXPERIMENTAL

a) Purification of starting material. 100 g of the commercially obtained deposit was recrystallized 3 times from 65% isopropyl alcohol. We obtained 71.5 g of lustrous, white plates. After drying in vacuum over P_2O_5 (85°, 2-4 mm), the substance had m.p. 214-215°; $[\alpha]^{20}D$ +7.25° (water, c 10.6).

Found %: C 49.2; H 7.62; N 7.55; S 8.42; SO''_4 26.25. $C_{15}H_{26}O_2N_2 \cdot H_2SO_4$. Calculated %: C 49.42; H 7.74; N 7.68; S 8.78; SO''_4 26.35.

b) Isolation of substance A. 10 g of the sulfate of substance A was dissolved in 100 ml of water with gentle heating. Powdered $Ba(OH)_2$ was added until there was an alkaline reaction to phenolphthalein. A stream of CO_2 was passed through the mixture until the alkaline reaction disappeared and then the mixture was filtered. The slightly turbid filtrate was purified with active charcoal. The colorless, clear solution was evaporated in vacuum. The dry residue was dissolved in 45 ml of methanol with heating. The solution was treated with activated charcoal. To the clear solution was added an equal volume of anhydrous acetone. A crystalline precipitate in the form of prisms began to form immediately. The weight was 6 g. After drying in vacuum (P_2O_5, 100°, 2-4 mm), the substance had m.p. 217-218°; $[\alpha]^{20}D$ + 14.2° (water, c 5.2).

Found %: C 67.80; H 9.77; N 10.39. $C_{15}H_{26}O_2N_2$. Calculated %: C 67.62; H 9.89; N 10.5.

Substance A was insoluble in chloroform, ether, acetone and dioxan difficultly soluble in anhydrous alcohol, more soluble in 95% alcohol, still more soluble in methanol and readily soluble in water.

By mixing alcohol solutions, we obtained a picrate with m.p. 175-176°.

Found %: N 14.17%. $C_{15}H_{26}O_2N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 14.15.

On acidification of a solution of substance A in methanol with an alcohol solution of HCl (to congo) followed by the addition of acetone, a crystalline precipitate of the dihydrochloride was formed and this had m.p. 252-253° (decomp.), $[\alpha]^{20}D$ +6.4° (water, c 4.4).

Found %: C 52.83; H 8.69; N 7.34; Cl 18.66. (for air-dried material). $C_{15}H_{26}O_2N_2 \cdot 2HCl \cdot C_2H_5OH$. Calculated %: C 52.95; H 8.87; N 7.27; Cl 18.41.

2 g of substance A was dissolved in 30 ml of a 50% solution of HCl in methanol. The solvent was distilled off the following day and the hydrochloride recrystallized from 10 ml of methanol. We obtained 1.5 g of a salt, which was dissolved in water, made alkaline and extracted with ether to give the free base (an oil). Solution of the latter in ethyl acetate gave 0.7 g of the crystalline methyl ester of substance A with m.p. 81-82°. The addition of a methanol solution of HCl to a methanol solution of the substance obtained precipitated crystals of a hydrochloride with m.p. 233-235°.

c) Preparation of aphyllinic acid. A solution of 5 g of aphylline hydrochloride in 15 ml of water was made alkaline with 50% KOH and shaken with benzene (4 x 25 ml). Aphylline was extracted from the benzene solution with 7% H_2SO_4 (2 x 25 ml). The sulfuric acid solution was heated for 5 hours on a water bath. Then the solution was treated with barium hydroxide. The remaining aphylline was extracted from the filtered solution with benzene, then a stream of CO_2 was passed through the alkaline solution. The solution was then treated as described in experiment "b". We obtained 1.5 g of a crystalline precipitate of aphyllinic acid. After recrystallization from methanol, the acid had m.p. 217-218°. It did not depress the melting point of substance A.

1.5 g of aphyllinic acid was treated similarly to substance A in the preparation of its methyl ester (see experiment "b"). We obtained 0.3 g of methyl aphyllinate with m.p. 82-83°. The ester did not depress the melting point of the methyl ester of substance A.

By mixing alcohol solutions of methyl aphyllinate and picric acid we obtained a monopicrate as long yellow needles with m.p. 221-222° (decomp.).

Found %: N 13.49. $C_{16}H_{28}O_2 \cdot C_6H_3O_7N_3$. Calculated %: N 13.79.

d) Preparation of aphyllidinic acid. A solution of 1.9 g of aphyllidine with m.p. 111-112° in 20 ml of 7.5% H_2SO_4 was heated on a water bath for 5 hours. The product was isolated as described in experiment "b". The amino acid was purified by reprecipitation with acetone from a methanol solution. We obtained 1.1 g of aphyllidinic acid in the form of octahedrons. After drying in vacuum (P_2O_5, 60°, 2-4 mm), the substance had m.p. 215-216° (decomp.); $[\alpha]^{20}D$ −8.0° (methanol, c 7). In a test for unsaturation with $KMnO_4$ and H_2SO_4, the reagent was immediately decolorized.

Found %: C 68.0; H 9.21; N 10.4. $C_{15}H_{24}O_2N_2$. Calculated %: C 68.13; H 9.15; N 10.59.

Mixing alcohol solutions of aphyllidinic and picric acids gave an amorphous yellow precipitate. Recrystallization from dilute alcohol with slow cooling, gave short, broad crystals with m.p. 196° (decomp.).

Found %: N 15.40. $C_{15}H_{24}O_2N_2 \cdot 2C_6H_3O_7H_3$. Calculated %: N 15.5.

e) Isolation of aphyllinic and aphyllidinic acids from technical anabasine sulfate. To 250 g of technical anabasine sulfate (which was obtained from the process when significant amounts of aphylline acid sulfate were produced) was added 50% sulfuric acid until there was a strongly acid reaction to methyl orange. The mixture was left for 2 days and then filtered. The residue on the filter was washed with isopropyl alcohol and recrystallized twice from a 65% aqueous solution of the latter. We obtained 25 g of white plates, identical with aphyllinic acid sulfate. To the filtrate (without the wash alcohol) was added water up to 700 ml and then $Ba(OH)_2$ to a strongly alkaline reaction to phenolphthalein. The precipitate of $BaSO_4$ was filtered off. The filtrate was evaporated down to 250 g in vacuum. The alkaloids were almost completely extracted with chloroform. A stream of CO_2 was passed through the alkaline aqueous solution until there was a neutral reaction to phenolphthalein. The precipitate was separated off and the filtrate evaporated to dryness in vacuum. The brown amorphous residue (17 g) was dissolved in 50 ml of methanol and the solution purified with activated charcoal. The filtrate was concentrated to to 35 ml and an equal volume of anhydrous acetone was added to it. The crystalline precipitate formed (2.75 g) was dissolved in 5 ml of CH_3OH with heating. To the solution was again added an equal volume of acetone. Crystals (octahedrons) of aphyllidinic acid with m.p. 215-216° were gradually deposited.

f) Preparation of aphylline from aphyllinic acid. 15 g of aphyllinic acid in a pyrex flask was heated on a bath at 225-235° for 25 minutes. Cooling gave a thick, brownish oil, which was completely dissolved in benzene. The solution was passed through a column containing 100 g of Al_2O_3. The column was eluted with benzene. In all the fractions was a thick, light oil (12.5 g in all). Solution in anhydrous alcohol and the addition of alcoholic HCl yielded crystals of a hydrochloride with m.p. 210-213° (decomp.); $[\alpha]^{20}D$ +11.3° (water, c 3.7). 5.5 g of the hydrochloride obtained was dissolved in water, made alkaline, extracted with petroleum ether, dried with potassium carbonate and distilled to give 4.3 g of a basic oil, which distilled at 185-190° (2-3 mm), $[\alpha]^{20}D$ +13.1° (methanol, c 15.6). By mixing alcohol solutions of this base and picric acid, we obtained crystals with m.p. 230-231° (decomp., from methanol). A mixed melting point with the obtained hydrochloride and the hydrochloride of aphylline and also with the obtained picrolonate and the picrolonate of aphylline was not depressed.

g) Preparation of aphyllidine from aphyllidinic acid. 1.5 g of aphyllidinic acid in a Claisen flask was heated at 220-230° for 20 minutes in a stream of nitrogen. The molten mass was distilled (bath temperature 150°, pressure 2-4 mm). An oil (0.5 g) was distilled and this was dissolved in petroleum ether, chromatographed on Al_2O_3 and eluted with petroleum ether to give crystals (0.25 g) with m.p. 107-108°. After purification via the perchlorate, the substance had m.p. 110-112°. It did not depress the melting point of aphyllidine.

h) Preparation of a new base, isomeric with aphylline. 12.5 g of aphyllinic acid hydrochloride was heated at 265-270° for 25 minutes. The mass melted and gaseous products were evolved. Cooling yielded a light brown glassy mass, which was dissolved in water (the solution gave an acid reaction). The solution was washed with chloroform, made alkaline and extracted with ether. Evaporation of the ether gave a thick brown oil (6.5 g). The oil was dissolved in benzene, chromatographed on Al_2O_3 and eluted with benzene. From the first fractions we obtained 3.1 g of a semicrystalline residue. The residue was sublimed in vacuum (100°, 2-4 mm). We obtained 2.5 g of white, but slightly oily crystals, which were recrystallized twice from hexane. The m.p. was 105-106°, $[\alpha]^{20}D$ +25.9° (anhydrous alcohol, c 14).

Found %: C 72.30; H 9.57; N 11.10. $C_{15}H_{24}ON_2$. Calculated %: C 72.52; H 9.75; N 11.28.

A picrate was prepared by the usual method; it formed yellow needles with m.p. 179-180° (decomp.; from ethanol). The perchlorate formed plates with m.p. 233-234° (decomp.).

1.8 g of aphylline hydrochloride was heated for 30 minutes at 250-265°. The reaction mixture was dissolved in 10 ml of dilute hydrochloric acid and extracted with ether after being made alkaline. Evaporation of the ether gave 1 g of a yellow oil, from which substance B was obtained by the method described above.

SUMMARY

1. The crystalline substance, which separates during the production of anabasine sulfate, consists mainly of aphyllinic acid sulfate, formed during the production process by the action of sulfuric acid on aphylline.

2. Aphyllidinic acid was prepared and described for the first time.

3. The possibility of obtaining aphylline in quite good yield by heating aphyllinic acid to melting was demonstrated.

4. In investigating the product obtained by melting aphyllinic acid hydrochloride, a crystalline substance was isolated, which was isomeric with aphylline. The same substance was obtained by melting aphylline hydrochloride.

Received January 16, 1957

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STEROID SAPOGENINS

III. THE SAPOGENINS OF THE RHIZOMES AND LEAVES OF YUCCA FILAMENTOSA FROM THE BLACK SEA COAST OF CAUCASIA

O. S. Madaeva

The literature contains extensive material on the study of the composition of sapogenins obtained by hydrolyzing saponins, extracted from various types of yuccas [1-10]. We investigated the rhizomes and leaves of Yucca Filamentosa from the Black Sea coast of Caucasia, which were given to us by the All-Soviet Institute of Medicinal and Aromatic Plants (VILAR).

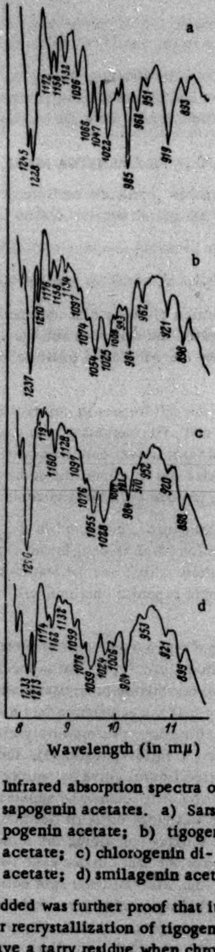
It is known [5] that examples of this type of yucca are outstanding in the differences in composition of the sapogenins obtained. 1.1% of gitogenin [9] was isolated from the rhizomes of Y. filamentosa growing in California; in addition to gitogenin, tigogenin and traces of mexogenin were extracted from leaves collected in southern France [4] and, finally, the Czech scientist Cerny [10], whose work was carried out at almost the same time as ours, reported that the leaves of Y. filamentosa growing in Czechoslovakia, yielded 0.72% of tigogenin.

We extracted and hydrolyzed the saponins from the rhizomes of Y. filamentosa (collected in the autumn of 1953 in Tsikhisdziri) basically by Wall's method [11], substituting methanol for ethyl alcohol in the extraction; the aqueous, fat-free solution of the saponins gave a colored, friable precipitate which was the water-insoluble saponins. The results of the detailed study of the nature of the water-insoluble saponins obtained will be reported separately.

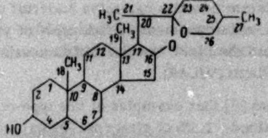
The aqueous saponin solution was extracted with butanol to free it from sugars and traces of protein. After distilling off the butanol, the aqueous solution was hydrolyzed with 4 N hydrochloric acid. The sapogenin mixture was washed with cold alcohol and light petroleum ether and formed a white, crystalline precipitate, whose chloroform solution did not give a yellow color with tetranitromethane, indicating that the sapogenins had a saturated character. After crhomatography on aluminum oxide and repeated recrystallization, this mixture yielded a precipitate which in elementary composition, melting point and R_f corresponded to sarsasapogenin (I): the acetate obtained had an IR-spectrum characteristic of sarsasapogenin acetate [12] (see figure, curve a), and corresponded to it in elementary composition. It is known [13] that sapogenins of similar polarity cannot be separated clearly on aluminum oxide; thus the separation of a second monohydroxysapogenin was quite difficult but these difficulties were eliminated by using paper partition chromatography extensively. The eluates containing the same sapogenins were separated by the results of paper chromatography. The chromatograms of the last eluates gave two large spots – one in the region of ketosapogenin, which was closer to the starting line, and the other spot corresponded to the less polar, saturated monohydroxysapogenin. Using Girard T reagent,two sapogenins were isolated from this mixture and identified as tigogenin (II) and hekogenin (III); their acetates were prepared and compared with appropriate samples of pure sapogenins. The IR-spectrum of tigogenin acetate, of which a small amount was obtained, coincided completely with the IR-spectrum of authentic tigogenin acetate [13] (see figure, curve b).

It should be noted that an attempt to separate the sapogenins from the rhizomes of Y. filamentosa without purifying the saponins with butanol, resulted in strong carbonization during hydrolysis and the sapogenins could not be obtained practically.

Saponins were also extracted from the leaves of Y.filamentosa (collected in March 1955 in Kobulet) in a Soxhlet apparatus with 80% methanol and defatted with dichloroethane. Sapogenins isolated from saponins that had been purified with butanol were less tarry than those from saponins not treated with butanol. However, a pure sapogenin could not be obtained by recrystallization; apparently this was due to the traces of other sapogenins, which were later detected chromatographically. To isolate and purify the sapogenins chromatographically we checked the conditions proposed by Wall [13, 14] and Cerny [10]. A comparison of the chromatographic results showed that, using the second method, developed by the Czech scientist (elution with ether), resulted in the separation of the monohydroxysapogenins from the tarry impurities, while in using the first method (washing with chloroform, a more polar solvent), the tarry impurities came out with the monohydroxysapogenins. The residues from the ether eluates gave pure tigogenin after one recrystallization, while the recrystallized tigogenin, isolated from the chloroform eluates, had a lower melting point.



Infrared absorption spectra of sapogenin acetates. a) Sarsasapogenin acetate; b) tigogenin acetate; c) chlorogenin diacetate; d) smilagenin acetate.



I) Sarsasapogenin – 5β,25 L-spirostan-3β-ol [11];
II) tigogenin – 5α,25 D-spirostan-3β-ol;
III) hekogenin – 5α,25 D-spirostan-12-one,3β-ol;
IV) gitogenin – 5α,25 D-spirostan-2α,3β-diol;
V) chlorogenin – 5β,25 D-spirostan-3β,6β-diol;
VI) smilagenin – 5β,25 D-spirostan-3β-ol.

After isolation of the tigogenin the column was eluted with methanol; the crystalline precipitate obtained from the methanol eluates, when chromatographed on paper with solvents for sapogenins of group I [15], gave one spot near the starting line; according to the R_f value it could belong to a dihydroxysapogenin. A comparison of the chromatogram of this substance with those of pure samples of gitogenin (IV) and chlorogenin (V) showed that it gave a spot which had an R_f value identical to that of chlorogenin. The IR-spectrum of its acetylation product was identical to the IR-spectrum of chlorogenin diacetate (see figure, curve c); in addition, the appearance of a yellow color when a drop of concentrated sulfuric acid was added was further proof that it was chlorogenin, as under these conditions gitogenin gave a purple color [16]. After recrystallization of tigogenin from a mixture of benzene and hexane (1 : 1), the residue from the filtrates gave a tarry residue when chromatographed on a column with aluminum oxide; this tarry residue gave one spot on the chromatogram with a greater R_f value than that of tigogenin. After acetylation, its IR-spectrum had bands characteristic of smilagenin acetate (VI; curve d).

The IR-absorption spectra were obtained in the physical chemistry laboratory under the supervision of Iu. N. Sheinker and we would like to thank him.

EXPERIMENTAL

For paper chromatography we mainly followed the method in [15], which had been changed slightly [17].

The work was carried out with rhizomes and leaves, which had been dried in air. These were ground and passed through a sieve with 3 mm holes.

Isolation of sapogenins from rhizomes of Y. filamentosa. 600 g of ground rhizomes were exhaustively extracted with 80% methanol in a Soxhlet apparatus for 3 days (a test of the residual plant material for hemolysis was negative). The methanol was distilled off and an equal volume of alcohol added to the residue, which was extracted with benzene, saturated with 50% alcohol. The alcohol was distilled off from the aqueous alcohol solution of the saponins; on standing the residue gradually deposited a precipitate of the water insoluble saponins. The precipitate was filtered off and washed with water; it did not dissolve in ether, dissolved slightly in alcohol and more so in hot butanol and did not deliquesce in air. Drying at 100° yielded 5.4 g of a fine, reddish powdery precipitate. The precipitate was not examined further; it was only hydrolyzed with acid. Paper chromatography of the sapogenins obtained gave only a spot with an R_f in the region of monohydroxysapogenins.

After hydrolysis of the water soluble saponins, freed from sugars by extraction with butanol, we obtained 8.5 g of a light yellow, tarry residue, which completely crystallized on being ground with alcohol. When washed with cold alcohol and petroleum ether, it became almost colorless; the m.p. was 178-182°. For purification 2.7 g of this precipitate was dissolved in 50 ml of dry benzene (thiophene free), containing 2% chloroform, and chromatographed on 38 g of aluminum oxide. The column was eluted using a gradually increasing chloroform content and then with chloroform alone. After several recrystallizations from methanol, ether and acetone, the residue isolated from the chloroform eluates corresponded to sarsasapogening (I) in R_f value. The m.p. was 197-199°; literature data: m.p. 199-200°, 200° [11, 18].

Found %: C 77.79; H 10.36. $C_{27}H_{44}O_3$. Calculated %: C 77.80; H 10.6.

Sarsasapogenin acetate. 1.5 g of impure sapogenins with m.p. 180-183°, 2.5 ml of pyridine and 12 ml of acetic anhydride were boiled for 30 minutes. A precipitate formed after cooling; the liquid was removed from it and the precipitate was washed with water, dried and recrystallized twice from methanol and then from acetone. The m.p. was 143-144°, $[\alpha]^{20}D$ −72° (c 1; $CHCl_3$); literature data: m.p. 128-130° [15], 138-142° [1], 144-145° [11], $[\alpha]^{20}D$ −71° ($CHCl_3$) [15].

Found %: C 75.84, 75.81; H 10.01, 10.00. $C_{29}H_{46}O_4$. Calculated %: C 75.94; H 10.11.

Tigogenin (II). 5 g of the mixture of sapogenins with m.p. 178-181° was dissolved in 100 ml of chloroform, placed in a column of 105 g of aluminum oxide and washed with 65 ml portions of chloroform to give 52 eluates. On paper, the first 7 eluates showed only a spot close to the solvent front; it was not possible to identify a substance from them. The following 10 eluates gave two spots − one on the level of the spot from the first seven eluates and the second corresponding to sarsasapogenin (R_f 0.89; total weight of residues, 0.7 g). On the chromatograms of the 18th to the 40th eluates were found three spots − two spots on the levels of the spots of the previous eluates and the third corresponding to tigogenin (R_f 0.71; total weight of residues of these eluates, 1.2 g). We were unable to isolate pure tigogenin from these by crystallization. The last eluates (from the 41st to the 52nd) gave two spots − one large one with R_f 0.71 and the second, a new one close to the starting line with R_f 0.34; from its position it corresponded to a ketosapogenin (total weight of residues, 2 g). Further washing of the column with chloroform with methanol added gave a tarry solution; its paper chromatogram showed that it contained a mixture of the sapogenins found above. These residues were not examined.

1.75 g of the residues of the combined eluates from 41 to 50 was treated with Girard T reagent. From the nonketonic fraction we obtained 1.16 g of a yellowish residue, which was washed with ether. After recrystallization from acetone the substance had m.p. 198-202°; R_f 0.71, like the sample of tigogenin from the Prague Chemical Institute of the Czechoslovakian Academy of Sciences; a mixed melting point was not depressed. Literature data: m.p. 201-202° [15], 206 [18]. The tigogenin acetate obtained from it had m.p. 202-204°; literature data: 195-197° [15], 206-208° [11]. The IR-spectrum corresponded to the IR-spectrum of tigogenin acetate [13].

Hekogenin (III). The aqueous solutions after the separation of the nonketonic fraction was acidified with hydrochloric acid to give 0.5 g of a slightly colored precipitate, which had m.p. 254-258° after two recrystallizations from acetone and then one from ethyl acetate. A paper chromatogram showed a spot identical in R_f value to a sample of pure hekogenin; a mixed melting point with hekogenin, isolated from Agave Americana (see report V) was not depressed. Literature data: m.p. 245, 253, 268° [1] and 245-247° [15]. The hekogenin acetate had m.p. 243-245°; literature data: 243°, 252° [1], 245° [11]. Its IR-spectrum was in complete agreement with the IR-spectrum of hekogenin acetate [12]. In elementary analysis it corresponded to hekogenin acetate.

Isolation of sapogenins from the leaves of Y. filamentosa. 220 g of powdered leaves was extracted in a Soxhlet apparatus with 80 % methanol; dichloroethane was used for defatting. After hydrolysis with 3 N hydrochloric acid and subsequent saponification with alcoholic alkali, 3.14 g of a tarry substance was obtained. Half of this (1.57 g) was chromatographed by Wall's method [13, 14] and from the chloroform eluates we obtained 1.2 g of a crystallizable oil, which was treated with ethyl acetate to give 0.42 g of crystals with m.p. 197.5-203°. The residue from the column was removed by elution with benzene, containing 30% alcohol. The second half of the tarry product (1.57 g) was chromatographed under the conditions described by Cerny [10]. The ether eluates yielded 1.01 g of a tarry residue, which gave 0.37 g of a solid with m.p. 202-204° after recrystallization. Paper chromatography of it gave one spot with R_f 0.71 and the filtrates from the recrystallization gave two spots – one with R_f 0.71 and a second with a larger R_f value. The residue from the column was washed out with a mixture of ether and alcohol. Tigogenin acetate, prepared from the tigogenin, was crystallized from acetone and washed with petroleum ether. The m.p. was 202-204°, $[\alpha]^{20}D$ −68.3°, −71° (c 1; $CHCl_3$); literature data: m.p. 204°, $[\alpha]^{20}D$ −73° [18]; m.p. 202-204°, $[\alpha]^{20}D$ −69° ($CHCl_3$) [10].

Found %: C 76.02; H 10.02. $C_{29}H_{46}O_4$. Calculated %: C 75.94; H 10.11.

SUMMARY

1. 0.45% of a mixture of sapogenins, consisting of sarsasapogenin, tigogenin and hekogenin was extracted from the rhizomes of Yucca filamentosa from the Black Sea coast of Caucasia.

2. 0.34% of tigogenin was obtained from the leaves of Y. filamentosa and it was shown that the leaves also contain chlorogenin and smilagenin.

Received February 7, 1957

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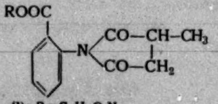
INVESTIGATION OF ACONITE ALKALOIDS

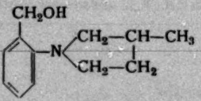
X. ELATINE. STRUCTURE OF ESTERIFYING ACID

A. D. Kuzovkov and A. V. Bocharnikova

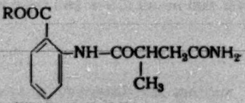
Hydrolytic cleavage of the alkaloid elatine gives the aminoalcohol elatidine [2] and methylsuccinylanthranilic acid [3]. In report (IV) [3], one of us proposed that in the molecule of elatine the carboxyls of methylsuccinic acid and the nitrogen of anthranilic acid formed an N-substituted methylsuccinimide grouping. On this basis, the partial formula (I) was proposed for elatine. We confirmed this proposal by studying the reduction of elatine with lithium aluminum hydride; in addition to elatidine, we obtained the base (II) with the composition $C_{12}H_{17}ON$, which was formed from elatine by reductive cleavage of one of the ester links and reduction of the two carbonyls of the methylsuccinyl group to methyl groups, which indicated [4] the presence of amide carbonyls in the esterifying acid of elatine. The reduction of elatine proceeded by the equation (I) ⟶ (II) + elatidine.



(I) $R=C_{26}H_{43}O_8N$
(III) $R=H$



(II)



(IV) $R=C_{25}H_{40}O_8N$

The base $C_{12}H_{17}ON$ may only be 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol (II) and the esterifying acid, consequently, has the formula (III). The acid structure corresponding to formula (III) was also proposed for the esterifying acid of the alkaloid methyllycaconitine by Cookson et al., [5] on the basis of spectrographic investigations. This work was carried out at the same time as our investigation of elatine.* The similarity of elatine and methyllycaconitine had been noted by us previously [3]. Apparently these alkaloids differ only in that elatine contains a dihydroxymethylene group instead of the glycol group of methyllycaconitine. By reduction of methyllycaconitine with lithium aluminum hydride, we obtained a base $C_{12}H_{17}ON$, identical with the base (II), obtained by the reduction of elatine. This confirmed the data of Cookson et al. on the structure of the esterifying acid of methyllycaconitine.

The presence of a substituted methylsuccinimide group in elatine and methyllycaconitine explains their instability towards ammonia and the ease of conversion [6] or methyllycaconitine into delsemine (IV). It is similar to the conversion of succinimide into succinamide [7]. The isolation of elatine and methyllycaconitine from plants has to be carried out without the use of ammonia. Thus, for example, the extraction of elatine with xylene from the plant Delphinium elatum, wetted with 5% soda solution, raises the yield of the alkaloid from 0.03 [2] to 0.15%. Methyllycaconitine hydroiodide may be obtained from Delphinium dictyocarpum D. C. [8]. Extraction with dichloroethane after wetting the dry plant with soda solution raised the yield to 0.7%; if ammonia is used as the alkali, delsemine may also be isolated from the combined alkaloids in addition to methyllycaconitine.

The similarity in the structure of elatine and methyllycaconitine causes the similarity in their pharmacological properties: both of them are curare-like preparations [9]; they also have an effect when administered internally and in this they are superior to curare-like substances containing quaternary nitrogen atoms. The curare-like properties are not connected with the presence of the succinimide group in the molecule of these alkaloids as these properties are also possessed by delsemine [10], avadkharidine* and ajacine.* Apparently, curare-like properties are inherent in esters of lycoctonine or amino alcohols close to it, esterified with N-acylated anthranilic acid.

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* Our fourth report [3] was received by the editor of the journal on April 23, 1954, and the work of Cookson et al., [5] in May, 1954.

EXPERIMENTAL

Reduction of elatine. 4 g of elatine was placed in the thimble of a Soxhlet apparatus and a solution of 2 g of $LiAlH_4$ in 0.5 liter of absolute ether in the flask of the apparatus. The elatine was extracted for about 60 hours and then the reaction mixture was treated with excess 10% hydrochloric acid. The ether layer was extracted 3 times with 10% hydrochloric acid. The acid extracts were combined and made alkaline with NaOH with cooling until the aluminum hydroxide dissolved. The base was extracted from the alkaline solution with chloroform. After drying the extract with sodium sulfate and evaporating off the solvent, we obtained 3.5 g of a mixture of bases, from which elatidine crystallized when ether was added; the yield was 2.3 g. The solvent was removed from the mother liquors and the residue vacuum distilled to give 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol; the yield was 0.7 g.

B.p. 105-108° (0.1 mm), d^{20}_4 1.0799, n^{20}D 1.5652, MR 57.7; calc. 57.3; $[\alpha]^{20}$D +8.6° (c 2.8 in alcohol).

Found %: C 74.78; H 8.97; N 7.5; labile hydrogen 0.52. $C_{12}H_{17}ON$. Calculated %: C 75.36; H 8.96; N 7.35; labile hydrogen 0.53.

The picrate of 2-[N (3-methylpyrrolidyl)]-benzyl alcohol was prepared by mixing alcohol solutions of the base and picric acid and the salt was washed with alcohol on the filter and dried, when it had m.p. 103°.

Reduction of methyllycaconitine. 10 g of the base was dried by distillation of benzene from it and then it was dissolved in 0.5 liter of absolute ether and reduced with 4 g of $LiAlH_4$ (2 hours boiling). The mixture of bases, isolated like the reduction products of elatine, were dissolved in moist ether; at this lycoctonine cyrstallized and after drying it had m.p. 149° (in vacuum). It did not depress the melting point of a sample of lycoctonine, obtained by saponification of the alkaloid. From the mother liquor we isolated 1.6 g of 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol.

B.p. 108° (0.1 mm), d^{20}_4 1.0726, n^{20}D 1.5678, $[\alpha]^{20}$D +12.60° (c 2.5, in alcohol). The picrate had m.p. 104° and did not depress the melting point of the substance obtained from elatine.

SUMMARY

The esterifying acid of elatine and methyllycaconitine is 2-[N-(3-methyl-2,5-dioxopyrrolidyl)]-benzoic acid. The presence of a substituted succinimide group explains the instability of elatine and methyllycaconitine to ammonia.

Received February 7, 1957

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*According to data obtained by colleague, P. M. Dozortseva, at the All-Soviet Chemical Pharmaceutical Research Institute. "Avadkharidine" - as in original.

** See C. B. Translation.

*** Original Russian pagination. See C. B. Translation.

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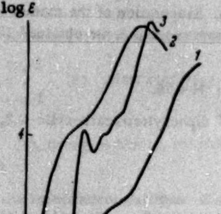
INVESTIGATION OF ACONITE ALKALOIDS

XI.* OXIDATION OF THE HYDROCARBON $C_{18}H_{18}$, FORMED DURING DEHYDROGENATION OF ZONGORINE **

A. D. Kuzovkov

The hydrocarbon $C_{18}H_{18}$ was obtained previously [2] in the dehydrogenation of zongorine with selenium and a hypothesis was put forward that this hydrocarbon was a trialkylphenanthrene. To find the position of the alkyl groups in hydrocarbon $C_{18}H_{18}$, it was oxidized with potassium ferricyanide under the conditions used by Ruzicka et al., [3] for oxidizing retene to a mixture of phenanthrenedicarboxylic-1,7 acid and diphenyltetracarboxylic-2,3,2',4' acid. When oxidized, hydrocarbon $C_{18}H_{18}$ also gave two acids which were isolated in the form of their methyl esters; ester (I) $C_{20}H_{18}O_8$, m.p. 150.5-151°; ester (II) $C_{20}H_{16}O_6$, m.p. 227-229°.



Ultraviolet absorption spectra (in alcohol). 1) Ester (I), methyl ester of diphenyltetracarboxylic-2,3,2',4' acid; 2) ester (II), methyl ester of phenanthrenetricarboxylic-1,7,9 (or 10) acid; 3) hydrocarbon $C_{18}H_{18}$.

In composition ester (I) corresponds to the methyl ester of a diphenyltetracarboxylic acid. The melting point of the ester coincides with that of the dimethyl ester of diphenyltetracarboxylic-2,3,2',4' acid. For comparison, the latter substance was synthesized by known methods: β-methylnaphthalene was converted to 1,7-dimethylphenanthrene [4], which was oxidized to diphenyltetracarboxylic-2,3,2',4' acid [3]. The methyl ester of this acid was identical to ester (I).

The infrared spectrum of ester (II) has a band, characteristic of ester carbonyl groups (1720 cm^{-1}); there are no hydroxyl group and keto group bands. One can conclude from this that all six oxygen atoms, in a molecule of the substance, belong to carbomethoxy groups. The composition of ester (II) corresponds to that of an ester of a phenanthrenetricarboxylic acid.

The character of the ultraviolet absorption of ester (I) (figure) indicates the presence of a closed phenanthrene nucleus in this substance. In going from hydrocarbon $C_{18}H_{18}$ to the ester of diphenyltetracarboxylic-2,3,2',4' acid, there is a sharp decrease in the absorption intensity, because of the destruction of the system of conjugated bonds of the phenanthrene nucleus. Ester (I) absorbs light more strongly than hydrocarbon $C_{18}H_{18}$ which indicates that the system of conjugated bonds of the phenanthrene nucleus remains and that a new conjugation of the nuclear double bonds with the carbonyl groups appears.

The results of oxidation confirm the hypothesis that hydrocarbon $C_{18}H_{18}$ is a trialkylphenanthrene; they also indicate that the alkyl groups in hydrocarbon $C_{18}H_{18}$ are in positions 1,7 and 9 or 10 of the phenanthrene nucleus, as only in this case can diphenyltetracarboxylic-2,3,2',4' acid be formed in addition to the phenanthrenetricarboxylic acid.

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*See [1] for previous report.

** "Zongorine" - as in original Russian text.

Phenanthrene hydrocarbons with substituents in positions 9 or 10 have not been detected up to now in the substances formed by the dehydration of aconite alkaloids. The detection of an alkyl group in hydrocarbon $C_{18}H_{18}$ in position 9 or 10 of the phenanthrene nucleus indicates either the presence of a substitutent in the corresponding nucleus in zongorine, or that this nucleus is seven- or eight-membered. During dehydrogenation such rings may be converted [5] into six-membered aromatic systems with new alkyl groups appearing at the contracted rings; the conversion may be facilitated by the presence of quaternary carbon atoms and a double bond in the molecule.

EXPERIMENTAL

0.5 g of hydrocarbon $C_{18}H_{18}$ and a solution of 100 g of potassium ferricyanide and 7 g of potassium hydroxide in 250 ml of water was heated and stirred at 90°. After being heated for 30 hours, the reaction mixture was treated with 40 g of potassium ferricyanide and 7 g of potassium hydroxide; heating and stirring were continued; after another 30 hours, a further 20 g of oxidant and 7 g of alkali were added. The total length of heating was 80 hours. After cooling, the precipitate of salts was filtered off and washed with ether and the filtrate extracted with ether. Drying and evaporation of the ether extract yielded about 0.05 g of unchanged hydrocarbon. The aqueous solution was acidified with hydrochloric acid. By extraction with ether, we obtained about 0.5 g of a crystalline mixture of acids, which was separated into two parts by trituration with methanol at room temperature: a)– insoluble in methanol (0.1 g) and b)– soluble in methanol (0.4 g). Esterification of part(a)with diazomethane in ether gave ester (II). For crystallization, the substance was dissolved in a small amount of chloroform and an equal volume of methanol added to crystallize out 50 mg of ester (II) with m.p. 227-229°.

Found %: C 68.20; 67.96; H 4.65, 4.52. $C_{20}H_{16}O_6$. Calculated %: C 68.18; H 4.58.

Part(b)was also esterified with diazomethane in ether solution. The reaction product was recrystallized from a large volume of methanol and this gave a small amount of ester (II). Evaporation of the mother liquor yielded a substance with m.p. 149-150°; after recrystallization of the latter from methanol, we obtained 15 mg of ester (I) with m.p. 150.5-151°.

Found %: C 62.02; H 4.79. $C_{20}H_{18}O_8$. Calculated %: C 62.20; H 4.70.

Ester (I) did not depress the melting point of the methyl ester of diphenyltetracarboxylic-2,3,2',4' acid. The two substances had identical infrared spectra.

SUMMARY

1. Oxidation of hydrocarbon $C_{18}H_{18}$ gave phenanthrenetricarboxylic-1,7,9 (or 10) acid and diphenyltetracarboxylic-2,3,2',4' acid.

2. It was shown that hydrocarbon $C_{18}H_{18}$ is a trialkylphenanthrene containing alkyl groups in positions 1,7 and 9 or 10 of the phenanthrene nucleus.

Received March 16, 1957

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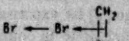
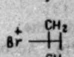
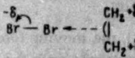
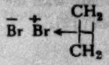
*Original Russian pagination. See C. B. Translation.

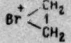
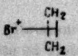
A DISCUSSION

IN REPLY TO THE "REMARKS" BY E. A. SHILOV [1]

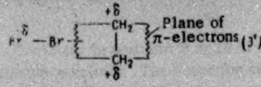
A. I. Titov and F. L. Makliaev

First of all the "Remarks" by E. A. Shilov should have been published in the Ukrainian Chemical Journal in 1955. In the original form of the article, E. A. Shilov wrote that Dewar [2] had considered a complex of an olefin and a halogen molecule  $Br \leftarrow Br \leftarrow \overset{CH_2}{\underset{CH_2}{\|}}$ (1). as an intermediate product. In our "Reply," it was stated that actually in the article quoted Dewar had written only of the bromine cation adduct with the hypothetical formula  $\overset{+}{Br} - \overset{CH_2}{\underset{CH_2}{\|}}$ (2): "π-complex in which bromine cations are linked to the π-electrons" [3]. E. A. Shilov is mistaken in identifying formula (2) with the structure we proposed for the complex of a halogen molecule with the olefin  $\overset{-\delta}{Br} - Br \leftarrow -- \overset{CH_2 +\delta}{\underset{CH_2 +\delta}{\|}}$ (3). After receiving our answer E. A. Shilov gave a second variation of Dewar's complex,  $\overline{Br}\ \overset{+}{Br} \leftarrow \overset{CH_2}{\underset{CH_2}{\|}}$ (4), trying as before, to make formula (4), at least superficially similar to our formula (3), and not noticing that the independent existence of the ions makes formula (4) and (2) identical.

In connection with this, we also changed our reply somewhat. In spite of the fact that both articles were quite ready, they were not published and E. A. Shilov preferred to send a third variation of "Remarks" to J. Gen. Chem.

The similarity we noted between the formula of Dewar's hypothetical cations of type (2) and the Roberts-Kimbal formula,  $\overset{+}{Br} < \overset{CH_2}{\underset{CH_2}{|}}$ (5), contrary to E. A. Shilov's opinion, is accepted by the majority of chemists. In particular, Dewar himself wrote [2]: "thus in the addition of bromine to a double bond the cyclic intermediate is probably  $Br^{+} - \overset{CH_2}{\underset{CH_2}{\|}}$" Knuniants, Kabachnik [4] et al., even assigned the Roberts-Kimbal structure directly to the π-complex. The similarity between these formulas consists basically of the fact that they represent an adduct, in which a bromine cation is chemically bonded to both carbon atoms of ethylene.

In our work carried out in 1943-46 [5, 6], with which E. A. Shilov is not familiar, complexes of halogen molecules with olefins were assumed to be the intermediate products of conjugated addition. The structure of these complexes we then represented as fully as possible by formula (3'), at which we arrived independently of Dewar's views.



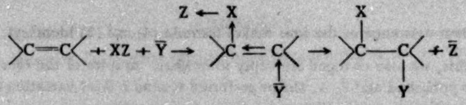
(3')

Its basic idea is identical to that of the more recent and concise formula (3), as both express the reaction caused by the introduction of π-electrons into the sphere of an electrophilic halogen molecule. The curve in formula (3) reflects the eccentric disposition of the density of π-electrons and their weaker bond to C nuclei, on which the peculiarities of the properties of the unsaturated compounds depend, and the sign ⟵ underlines the weak donor-acceptor bond of Br_2 and C_2H_4 in the complex; the correlation between the symbol for the semipolar bond and the sign ⟵ is approximately the same as that between the dash and the dotted line in the classical theory of valence. The use of a valence dash by Dewar to represent the bonds of the already generalized ethylene electrons, even with a cation, is incorrect; structure (1) and the formula given by E. A. Shilov for the adduct of HBr and ethylene [1] contradict even more the theory of valence and the symbols generally accepted. Other authors, in particular, O. A. Reutov [7] when discussing E. A. Shilov's results, have also concluded that it was advantageous to use the sign ⟵ for expressing the bonds of electrophilic molecules with π-electrons. Our ideas on the chemical nature of the initial reaction of olefins with halogens have now been confirmed by many other investigations [8].

We will not examine the similarity and difference between our mechanism of conjugated addition and one of Robinson's schemes, for the sake of brevity and also as two years ago [9] he expressed completely different views on the course of the reaction of bromine with ethylene, which have very little in common with the theory of conjugated addition. Naturally, features may be found in our ideas similar to the hypotheses of other authors, starting with Dumas (etherin theory), Lavoisier (murium hypothesis), Tile and finally Dewar.

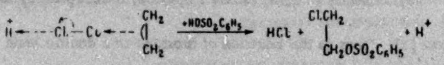
The idea introduced by us [5, 6] of "conjugated addition reactions" agrees with the facts observed – the drawing in of a third component into the reaction is related to the reaction of the halogen with the olefin. According to present day theory, the mechanism of conjugated reactions is actually characterized by the formation of labile complexes that react with a third component [10]. For differentiation, the type of process being examined may be defined, according to A. N. Nesmeianov [11], as the conjugated addition of halogens to olefins.

In our interpretation of the mechanism of conjugated addition of halogens to olefins [5, 6], the moving force of the reaction is clearly expressed as the formation of an electrophilic complex of a halogen molecule with the olefin, which is absent from the formal concept of E. A. Shilov of trimolecular coordinated reactions [12].



$$>C=C< + XZ + \bar{Y} \longrightarrow >\overset{\overset{Z \leftarrow X}{\uparrow}}{C} \Leftarrow \underset{\underset{\bar{Y}}{\uparrow}}{C}< \longrightarrow >\overset{\overset{X}{|}}{C}-\underset{\underset{Y}{|}}{C}< + \bar{Z} \qquad (6)$$

Starting with such a concept, it is doubtful if one could deduce that the strongest anhydrous acids could be involved in the reaction of halogens with olefins



$$\overset{+}{H} \leftarrow \cdots Cl-Cl \leftarrow \cdots \left(\begin{matrix} CH_2 \\ \| \\ CH_2 \end{matrix}\right. \xrightarrow{+HOSO_2C_6H_5} HCl + \begin{matrix} ClCH_2 \\ | \\ CH_2OSO_2C_6H_5 \end{matrix} + H^+ \qquad (7)$$

and, besides that, with greater success than the acids' salts. These reactions illustrate the unusually high alkalation capacity of complexes of halogens with olefins, which we first proved. They can in no measure be used as examples of the applicability of E. A. Shilov's scheme.

E. A. Shilov denies the possibility of the activating effect of sulfuric acid on the reaction of an aromatic nucleus with a halogen molecule, but this has been observed by many authors and should be considered as quite natural for all protonic and aprotonic acids. E. A. Shilov considers that the substitution of hydrogen atoms at π-bonds proceeds by a radical mechanism, but this is also baseless as it is contradicted, for example, by the extensive material on the chemistry of aromatic compounds. Without doubt, the conditions and results of the reactions we investigated correspond completely with the ionic mechanism assigned to them, and among them those for the side reaction of hydrogen substitution. We have not examined the mechanism of the reaction of acetylene on the surface of solid mercuric chloride and E. A. Shilov's remarks on this subject do not contradict our ideas and even enlarge somewhat the range of conjugated addition reactions. E. A. Shilov's objection to the use of letter coefficients for denoting chemical activity is best refuted by the fact that they are used, in particular, *f*, in work on reactivity; however, as is known, the meaning of the coefficient is determined not by its transcription but by the content.

In conclusion one must state that the first reason for E. A. Shilov's "Remarks" was an error. This error led him, as the above shows, to a series of baseless statements. Our contribution to the theory of conjugated addition, in particular, the substantiation of the probable role in them of complexes of halogen molecules with olefins, a rational exposition of their chemical structure, the illustration of the extremely high alkylation capacity of the complexes (even reacting with the strongest acids), the discovery and explanation of the orientation rules in conjugated additions, proof of the absence of a preliminary reaction of halogens with the third component etc., were ignored by E. A. Shilov and to belittle the synthesis achievements he called them preparative. Such results are rarely found in any, even prolonged, investigations on the reactions of halogens with olefins.

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Received September 2, 1957.

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*Original Russian pagination. See C. B. Translation.

** In Russian.

INVESTIGATION OF THE MECHANISM OF POLYCONDENSATION OF 1,3-DICHLOROBUTENE-2 IN THE PRESENCE OF FRIEDEL – CRAFTS – GUSTAVSON CATALYSTS. I.

A. L. Klebanskii, A. G. Saiadian and M. G. Barkhudarian

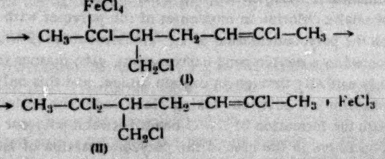
Polycondensation of 1,3-dichlorobutene-2 under the influence of Friedel – Crafts – Gustavson catalysts has been described in the Authors Certificate by Akopian, Saiadian and Barkhudarian [1]. No other literature data on this problem are available. Polymers of 1,3-dichlorobutene-2 are of interest as film-forming substances. In addition, polycondensation of 1,3-dichlorobutene-2 simulates in large measure the vulcanization of polychloroprene under the influence of metallic oxides.

We have investigated the polycondensation of 1,3-dichlorobutene-2 in the presence of $AlCl_3$, $FeCl_3$, $ZnCl_2$ and $SnCl_4$.

In all cases we found that low-molecular weight compounds were formed as well as resinous products. Polycondensation proceeds with the greatest efficiency in the presence of $AlCl_3$, with the formation of high-molecular weight polymers as the main products of the reaction. With $FeCl_3$ the process is slower and this gives rise to the formation of low-molecular weight products in considerable yields. $ZnCl_2$ approaches $FeCl_3$ in catalytic activity.* Dimers as well as low-molecular weight polymers were isolated from the reaction products. In the course of the examination of the composition and structure of the low-molecular weight constituents it was found that these contained the dimer ($C_8H_{12}Cl_4$) and a substance having the composition $C_8H_{11}Cl_3$.

At the present time, reactions catalyzed by Friedel – Crafts catalysts are interpreted in terms of an ionic mechanism involving the participation of so-called carbonium ions [2,3]. The mechanism of this reaction is considered in terms of the formation of addition complexes between the catalyst and the olefins. In the case of the molecule of 1,3-dichlorobutene-2 the shift of electron density brought about by the positive inductive effect of the methyl group and the conjugation of π-electrons of the double bond with the unpaired electrons on the chlorine atom renders the chlorine atom in position 1 highly reactive. The enhanced lability of this chlorine atom in its turn facilitates the formation with Friedel – Crafts catalysts of the complex $CH_3-CCl=CH-CH_2^+ \cdot FeCl_4^-$. The latter adds on to dichlorobutene according to the scheme

$$FeCl_4^- \cdot CH_2^+-CH=CCl-CH_3 + CH_3-CCl=CH-CH_2Cl \rightarrow$$



$$\rightarrow CH_3-\overset{\overset{\displaystyle FeCl_4}{|}}{C}Cl-\underset{\underset{\displaystyle CH_2Cl}{|}}{C}H-CH_2-CH=CCl-CH_3 \rightarrow$$

(I)

$$\rightarrow CH_3-CCl_2-\underset{\underset{\displaystyle CH_2Cl}{|}}{C}H-CH_2-CH=CCl-CH_3 + FeCl_3$$

(II)

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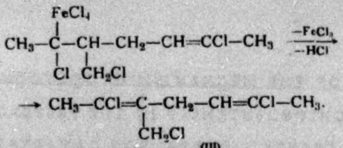
* The problem of the relative efficiency of different catalysts and of their influence on the yield of low- and high-molecular weight products resulting from the polycondensation will be discussed in greater detail in connection with our investigation of the preparation of film-forming substances based on polymers of 1,3-dichlorobutene-2.

The dimer, 2,6,6-trichloro-5-chloromethylheptene-2, has, in fact, the structure (II) which has been proved by ozonolysis. In the decomposition products of the ozonide we have found acetic acid (80% of the theoretically possible amount), β-chloromethyl-γ-dichlorovaleric acid (62.9%) and hydrochloric acid (91%).

The substance with the formula $C_8H_{11}Cl_3$ is apparently formed as a result of the simultaneous splitting of $FeCl_3$ and HCl from the complex



$$\mathrm{CH_3-\overset{FeCl_4}{\underset{Cl}{C}}-\underset{CH_2Cl}{CH}-CH_2-CH{=}CCl-CH_3} \xrightarrow[-HCl]{-FeCl_3} \mathrm{CH_3-CCl{=}\underset{CH_2Cl}{C}-CH_2-CH{=}CCl-CH_3}.$$

(III)

Among the products of ozonolysis of the substance $C_8H_{11}Cl_3$ we found acetic acid (80% of theory), hydrochloric acid (79.8%), chloroacetone (83.7%) and carbon dioxide (84%). The latter compounds are the products of the decomposition of γ-chloroacetoacetic acid which has not been isolated because of its instability. On the basis of these data it may be accepted as proved that the substance has the structure (III), i.e. the splitting off of HCl involves the tertiary carbon atom. The dimer of 1,3-dichlorobutene-2 (II) was polymerized in the presence of $FeCl_3$. In addition to various polymers, compound (III) was isolated from the reaction mixture.

The identity of 1,3-dichlorobutene-2 formed in the polycondensation as well as that of the products of the combination of two molecules, formed through the splitting off of HCl under the influence of $FeCl_3$, has been fully confirmed by analysis and ozonolysis. These results show that polycondensation of 1,3-dichlorobutene-2 takes place in a step-wise manner: first, there is combination of two molecules of 1,3-dichlorobutene-2, followed by the splitting off of HCl from the dimer (II); the resulting unsaturated compound (III) combines with a second molecule of 1,3-dichlorobutene-2; this is again followed by the splitting off of HCl with the formation of a new unsaturated compound, and so on. However, these results still only give an incomplete picture as regards the direction of the addition of the catalyst and of the nature of the splitting off of HCl from polymers of higher molecular weight.

The polymer distribution was determined by fractional precipitation with methanol from benzene solution. Among the products of decomposition of the ozonides of these fractions we detected carbon dioxide, acetic acid and a resinous product the structure of which could not be established. In view of the fact that with increasing complexity of the molecules the number of possible directions of the combinations of these molecules increases, it was found necessary to abandon the investigation of the structure of the high molecular weight products and to limit the investigation to the separation of these polymers into narrow fractions which were submitted to detailed analysis. The results obtained, from the investigation of the structure of compounds found by polycondensation of 1,3-dichlorobutene-2 under the influence of Friedel-Crafts catalyzates, provide a basis for the interpretation of the mechanism of vulcanization of polychloroprene under the influence of metallic oxide. As has been demonstrated in a number of investigations [3, 4], vulcanization of polychloroprene proceeds through the interaction of the allylic chlorine formed as a result of 1,2-addition (followed by isomerization of the tertiary chlorine atom into an allylic one) to the metallic oxides (MgO, ZnO, Fe_2O_3, etc.). Monomer units containing allylic chlorine amount to 1.5-2% of the polymer.

The mechanism of the vulcanization of polychloroprene is at present still insufficiently understood. It might be thought that this mechanism is based on the formation of an oxygen link between individual chains as a result of the interaction of allylic chlorine in molecules of the polymer with metallic oxides. However, the above experimental data on the polycondensation of 1,3-dichlorobutene-2 which contains allylic chlorine as well as a chlorine atom attached to a double bond carbon atom, give reasons to suppose that vulcanization of polychloroprene proceeds only partially through an oxygen bridge, and this only in the initial stage of the reaction. The subsequent mechanism is a polar one taking place under the action of the metallic chlorides formed ($ZnCl_2$, $FeCl_3$, etc.), with the formation of C – C bonds between polymer chains in accordance with the same mechanism which is operative in the case of the polycondensation of 1,3-dichlorobutene-2, i.e. through the addition of carbon atoms with an allylic chlorine in one chain to the double bonds of a second molecule, followed by the splitting off of HCl which gives rise to the formation of $ZnCl_2$.

EXPERIMENTAL

254 g of 1,3-dichlorobutene-2 was heated on an oil bath at the boiling point during 14 hours in the presence of 0.825 g of $FeCl_3$. The reaction was accompanied by the evolution of HCl. On fractionation in vacuo, after previous separation of unreacted 1,3-dichlorobutene-2, the following fractions were obtained: fraction 1, 80-100°/5 mm, 22.84 g; fraction 2, 100-115°/5 mm; residue polymer, 25.3 g. After a second distillation of fraction 1 there was obtained 9.2 g of compound (I) boiling at 91-93°/5 mm.

d^{20}_4 1.189, $n^{20}D$ 1.500, MR_D 52.71; Calculated, 52.90

Found, %: Cl 49.16, Cl (saponifiable) 16.40. $C_8H_{11}Cl_3$F. Calculated, %: Cl 49.88, Cl (sapon.) 16.62. Unsaturation was determined with 0.1 N bromine solution in chloroform. Found, 1.436 g Br_2 per 1 g of compound. Calculated 1.497 g Br_2.

6.84 g of compound (I) was taken for ozonolysis. Ozonolysis was carried out in solution in purified chloroform at -20°. On decomposing the reaction product with water there was evolution of CO_2 which was absorbed in 1 N solution of $Ba(OH)_2$; there was obtained 4.009 g of barium carbonate, which corresponds to 0.894 g of CO_2. The ozonolysis product passed almost entirely into solution in water, with the exception of a small amount of a resinous substance (0.1 g). Water was removed in vacuo (58 – 60° at 150 mm); and the residue contained 0.13 g of resin, making a total of 0.25 g. The acids contained in the aqueous distillate (174.4 g) were then determined. Total acidity was equivalent to 5.66 g KOH. No formic acid was detected ($AgNO_3$ test). Hydrochloric acid was determined by the Volhard method. The distillate contained 1.816 g (79.8%) of HCl.

The aqueous solution was divided into two portions in one of which acetic acid was determined. To this portion was added freshly prepared Ag_2O. The precipitate of AgCl was filtered off and the solution containing the silver salts was evaporated to dryness. The crystalline residue was purified by recrystallization and dried in vacuo to constant weight; the mother liquors were evaporated to dryness in vacuo and the crystals which separated were again recrystallized. Analysis of the crystals showed that the silver salt composition corresponded to silver acetate; no other salts were found.

Found %: Ag 63.08. $C_2H_3O_2Ag$. Calculated %: Ag 64.58

In view of the absence of other acids it appeared possible to calculate the amount of acetic acid from the total acidity of the aqueous distillate. The total distillate required 5.6627 g KOH for neutralization, of which 2.7856 g was required to neutralize the hydrochloric acid, while 2.8771 g KOH was used up by the acetic acid which corresponds to 3.08 g (80%) of acetic acid. The second portion of the aqueous extract was treated with 10% sodium carbonate to weakly alkaline reaction, followed by extraction with ether. After removing the ether there was obtained 1.2 g of chloroacetone.

Found %: Cl 37.78. C_3H_5OCl. Calculated %: Cl 38.38.

Interaction with 2,4-dinitrophenylhydrazine gave orange crystals, m.p. 126 – 127°; literature, m.p. 124 – 125.5° [5].

Found %: Cl 12.83. $C_9H_9O_4N_4Cl$. Calculated %: Cl 13.92.

The content of chloroacetone in the extract was determined by reaction with hydroxylamine hydrochloride and was found to be 97.3%. From the amounts of CO_2 and chloroacetone obtained the yield of γ-chloroacetic acid was calculated to be 2.7613 g (83.6%).

Fraction No. 2 yielded 18.2 g of substance boiling at 105-107°/5 mm.

d^{20}_4 1.2824, $n^{20}D$ 1.508, MR_D 58.11; Calculated, 58.26.

Found %: Cl 56.09, Cl (ionizable) 28; M 245.9; 1 g of the substance absorbs 0.6373 g of bromine. $C_8H_{12}Cl_4$F. Calculated %: Cl 56.8, Cl (ionizable) 28.4. M 250; 1 g of the substance will absorb 0.6392 g Br_2.

9.25 g of the compound was taken for ozonolysis which was carried out in solution in chloroform. The reaction product was decomposed with a 3% hydrogen peroxide solution. After decomposition of the ozonide an oily product remained in the flask. The aqueous extract did not contain formic acid ($AgNO_3$ test). In order to determine any volatile acids the aqueous extract was distilled in vacuo (boiling point 60 – 62° at 160 mm). Hydrochloric acid was determined in the distillate (95.8 g) by titration (Volhard method). Content of HCl in the solution, 1.2305 g (91%).

An aliquot portion of the aqueous solution was treated with freshly precipitated Ag_2O. The precipitate of AgCl which formed was filtered off. Silver acetate was isolated from the filtrate.

Found %: Ag 64.11. $C_2H_3O_2Ag$. Calculated %: Ag 64.58.

Since no other silver salts were found, apart from silver acetate, the yield of acetic acid was calculated from the total acidity of the mixture of the volatile acids. The aqueous solution required 3.55 g of KOH for neutralization of which 1.887 g was used to neutralize the HCl; consequently, 1.663 g was used to neutralize acetic acid which corresponds to 1.78 g (80.1%) of the acid.

The oily residue left after separation of the aqueous layer, was distilled in vacuo. After a second distillation there was obtained 5.04 g (62.9%) of β-chloromethyl-γ-dichlorovaleric acid, which is sparingly soluble in water but easily soluble in aqueous alcohol and acetone.

B.p. 113 – 115°/5.5 mm, d^{20}_4 1.3648, $n^{20}D$ 1.4975, MR_D 47.03; Calculated 46.88.

Found %: Cl 47.30. Equivalent Weight 258.4. $C_6H_9O_2Cl_3$. Calculated %: Cl 48.52. Equivalent Weight 255.1.

Fractionation of the products of polycondensation of 1,2-dichlorobutene-2. 65.1 g of the polymer was submitted to fractionation. Methanol was added portion-wise to the benzene solution of the polymer and the following fractions were separated: fraction 1, 9.5 g, (15.45%), fraction 2, 25.09 g (40.77%), fraction 3, 8.7 g (14.15%), fraction 4, 18.21 g (29.63%). The characteristics of the fractions are given in the table below.

Fraction No.	M (cryosc., in benzene)		Cl content (%)		Ionizable Cl (%)		Unsaturation (in g Br_2) per 1 g of substance		Molecular formula
	found	calc.	found	calc.	found	calc.	found	calc.	
1	1528.85	1541.0	40.38	41.54	2.137	2.33	1.725	1.765	$C_{68}H_{86}Cl_{18}$
2	888.4	921.18	42.28	42.37	3.827	3.85	1.712	1.736	$C_{40}H_{51}Cl_{11}$
3	381.18	390.5	45.078	45.43	9.28	9.11	1.608	1.64	$C_{16}H_{21}Cl_5$
4	264.2	—	—	—	—	—	—	—	Mixture of dimers and trimers

For ozonolysis we took 7.26 g of fraction 3. On decomposing the ozonide with water there was evolution of carbon dioxide (0.0032 g, absorbed in 1.0 N $Ba(OH)_2$). The products of decomposition contained resinous substance. Formic acid was absent. Hydrochloric and acetic acids were present. Hydrochloric acid was determined as chloride, and the fraction yielded 2.422 g of HCl. Acetic acid was determined as the silver salt.

Found %: Ag 64.12. $C_2H_3O_2Ag$. Calculated %: Ag 64.58.

A similar procedure was followed in the examination of the condensation products of 1,3-dichlorobutene-2 in the presence of the catalysts $AlCl_3$, $ZnCl_2$ and $SnCl_4$. The investigations have shown that by comparison with $FeCl_3$ as the catalyst, an increased yield of high molecular weight products is obtained in the presence of $AlCl_3$, while in the presence of $ZnCl_2$ the reaction proceeds at a slower rate.

SUMMARY

1. Polycondensation of 1,3-dichlorobutene-2 in the presence of Friedel – Crafts – Gustavson catalysts has been investigated.

2. The primary reaction product is the combination of two molecules of 1,3-dichlorobutene-2 giving 2,6,6-trichloro-5-chloromethylheptene-2; hydrogen chloride is then split off from the latter, giving 2,6-dichloro-5-chloromethylheptadiene-2,5.

3. In addition to the above compounds, polymers of higher molecular weights are also formed. The composition of these polymers confirms the mechanism of condensation proposed.

4. The authors have proposed a mechanism of vulcanization of polychloroprene in the presence of metal oxides through condensation under the influence of metal chlorides formed during the reaction.

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Received March 5, 1957

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*Russian translation.

**In Russian.

INTERACTION OF 1,3-DICHLOROBUTENE-2 WITH CHLOROPRENE UNDER THE INFLUENCE OF FRIEDEL – CRAFTS – GUSTAVSON CATALYSTS. II.

A. L. Klebanskii, A. G. Saiadian and M. G. Barkhudarian

With the exception of α-haloesters [1-3], the addition of halogen derivatives to dienes has not been investigated sufficiently. The possibility of addition of tertiary butylene chloride and bromide as well as of crotyl chloride and bromide to divinyl has first been indicated in a patent [4]. Subsequently, A. A. Petrov and K. V. Leets [5] investigated the interaction of divinyl, isoprene and diisopropenyl with primary, secondary and tertiary halogen derivatives in the presence of zinc halides.

In conjunction with investigations which are being carried out by one of us on the synthesis of compounds simulating the fundamental structural types of synthetic rubbers, with a view to comparing their relative reactivities, we have undertaken a study of the interaction of crotyl chlorides of different structures with chloroprene, isoprene and divinyl.

In the present paper we describe the results of our investigation of the interaction of 1,3-dichlorobutene-2 with chloroprene in the presence of catalysts, namely, $AlCl_3$ and $FeCl_3$. In both cases we have observed the formation of low molecular weight compounds as well as resinous products.

When $AlCl_3$ is used as the catalyst the yield of the adduct of one molecule of 1,3-dichlorobutene-2 to one molecule of chloroprene is very small, although the total amount of the various products of condensation is greater in this case. On increasing the catalyst concentration (to over 1 mole-%) there takes place preferential formation of high molecular weight compounds, which makes the isolation of the primary product of reaction difficult. The relative proportions of the reactants affects greatly the composition of the reaction products, the yield of the primary adduct increasing with increasing excess of 1,3-dichlorobutene-2.

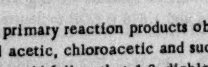
In order to investigate the reaction mechanism we have isolated the primary reaction products.

As is well known, interaction of the catalyst with 1,3-dichlorobutene-2 gives rise to the formation of a complex (e.g. $CH_3CCl{=}CHCH_2^{+} \cdot FeCl_4^{-}$) with a positively charged carbonium ion. The subsequent progress of the reaction depends on the interaction of this complex with chloroprene.

Addition of 1,3-dichlorobutene-2 to chloroprene may be expected to give rise to the formation of six different compounds as the primary products of the reaction:

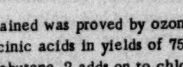
$CH_3CCl{=}CHCH_2CH_2CCl{=}CHCH_2Cl$ (I) $CH_3CCl{=}CHCH_2CH_2CH{=}CClCH_2Cl$ (II)

$CH_3CCl{=}CHCH_2CH_2CCl_2CH{=}CH_2$ (III) $CH_3CCl{=}CHCH_2CH_2CHClCCl{=}CH_2$ (IV)



$$CH_2ClCClCH{=}CH_2 \atop \quad\; |\, CH_2CH{=}CClCH_3$$

(V)

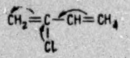


$$CH_2ClCHCCl{=}CH_2 \atop |\, CH_2CH{=}CClCH_3$$

(VI)

The structure of the primary reaction products obtained was proved by ozonolysis. Among the products of decomposition we found acetic, chloroacetic and succinic acids in yields of 75.6%, 80.3% and 81.09%, respectively. From this it would follow that 1,3-dichlorobutene-2 adds on to chloroprene either in the 1,4 or the 4,1 position (formulas I and II). Ozonolysis gives, however, no clue as to which of the two mechanisms is, in fact, operative, since in both cases acetic, chloroacetic and succinic acids are formed.

The most probable reaction mechanism may be established by a consideration of the distribution of electron density in the chloroprene molecule as depicted in formula (A).



(A)

This particular electron density distribution is confirmed by the mechanism of addition of HCl to chloroprene. This gives reasons to suppose that addition of the complex $CH_3CCl=CHCH_2^+ \cdot FeCl_4^-$ to chloroprene takes place in position 1,4.

In addition to compounds formed by the combination of one molecule of 1,3-dichlorobutene-2 and one molecule of chloroprene we have also isolated from the reaction products the adduct of 1,3-dichlorobutene-2 to two molecules of chloroprene. The composition of this adduct is expressed by the formula $C_{12}H_{16}Cl_4$. On the other hand, an adduct of two molecules of 1,3-dichlorobutene-2 to one molecule of chloroprene could not be detected among the products of the reaction.

The polymers were fractionated into narrow fractions by precipitation with methanol from benzene solution.

In the product of ozonolysis of the fraction having the composition $C_{20}H_{26}Cl_6$ we found acetic, chloroacetic and succinic acids. Analysis and ozonolysis show that this fraction is the condensation product of one molecule of 1,3-dichlorobutene-2 and four molecules of chloroprene.

We may, therefore, suppose that the interaction of 1,3-dichlorobutene-2 with chloroprene is a stepwise condensation: the primary product of the reaction is the adduct $CH_3CCl=CHCH_2CH_2CCl=CHCH_2Cl$, the next step being the formation of an adduct having the formula $CH_3CCl=CHCH_2(CH_2CCl=CHCH_2)_2Cl$, then $CH_3CCl=CHCH_2(CH_2CCl=CHCH_2)_3Cl$, and so on. Similar reactions have been described in the literature [6-8] and referred to as telomerization. Thus it appears that in the presence of 1,3-dichlorobutene-2 and under the influence of the catalysts $AlCl_3$ and $FeCl_3$, chloroprene undergoes a typical telomerization reaction.

EXPERIMENTAL

Interaction of 1,3-dichlorobutene-2 with chloroprene in the presence of ferric chloride. 62.5 g of 1,3-dichlorobutene-2 and 22.1 g of chloroprene and 1.285 g of $FeCl_3$ (1.0 mole-%) was kept in a sealed ampule, filled with nitrogen, at a temperature of 20° for 20 hours. In order to avoid further change of the reaction products during the subsequent treatment, the catalyst was removed by washing with 10% hydrochloric acid and water after which the residue was dried over $CaCl_2$. After removing the unreacted starting materials (13.1 g) the residue was fractionated in vacuo and the following fractions were collected: fraction 1, b.p. 95-110°/7 mm, 7.8 g; fraction 2, b.p. 130-150°/3 mm, 3.6 g; residue (polymer) 1.68 g. After a second distillation, fraction 1 yielded 4.2 g of substance with the following characteristics:

B.p. 101-103°/4.5 mm, d^{20}_4 1.2075, $n^{20}D$ 1.507, MR_D 52.64; Calculated 52.90.

Found %: Cl 49.50, ionizable Cl 16.02. M 206.55; bromine No. 147.2. $C_8H_{11}Cl_3$. Calculated %: Cl 49.88, ionizable Cl 16.68. M 213.5; bromine No. 149.7.

Ozonolysis was carried out with 8.55 g of the substance. After decomposition with water the resultant mixture of the acids did not contain any formic acid ($AgNO_3$ test). After removing the volatile acids in vacuo at 45-50° crystals of chloroacetic and succinic acids were left in the flask (6.87 g). The mixture of the volatile acids was found to contain 51.4% of the theoretical amount of HCl, as determined by determination of chloride by the Volhard method. An aliquot portion of the distillate was treated with freshly precipitated silver oxide. After separating the precipitate of silver chloride by filtration, the filtrate was evaporated in vacuo. The dry residue constituting the silver salt of the volatile acids was recrystallized and analysed.

Found %: Ag 63.92. $C_2H_3O_2Ag$. Calculated %: Ag 64.58.

Silver salts of other acids could not be detected. The amount of acetic acid was calculated from the total acidity of the mixed volatile acids. The distillate required total of 4.008 g KOH for neutralization, of which 2.31 g was used to neutralize the hydrochloric acid and 1.698 g KOH to neutralize acetic acid, which corresponds to 1.82 g (75.6%) of the latter acid.

From the crystalline residue there was obtained, by distillation, chloroacetic acid (b.p. 73-75° at 4.5 mm) in the form of white crystals melting at 61-62°. Literature, m.p. 61.5°.

Found %: Cl 37.02. Acid value 597. $C_2H_3O_2Cl$. Calculated %: Cl 37.57. Acid value 592.6.

The amount of chloroacetic acid obtained was calculated from the total chlorine content in the crystalline product (1.14 g), which corresponds to 3.04 g (80.3%) of chloroacetic acid.

The residual crystals of succinic acid (3.83 g, 81%) had a melting point of 180-181° after recrystallization. Literature, m.p. 182.3°.

Found: acid value 926.09. $C_4H_6O_4$. Calculated: 949.18.

After suitable treatment of fraction 3 there was obtained 1.5 g of a substance boiling at 140-142° at 3 mm.

Found %: Cl 46.81, ionizable Cl 11.25. M 289.5. $C_{12}H_{16}Cl_4$. Calculated %: Cl 47.02, ionizable Cl 11.76. M 302.

Interaction of 1,3-dichlorobutene-2 with chloroprene in the presence of aluminium chloride. Treatment of a mixture of 62.5 g of 1,3-dichlorobutene-2 and 22.1 g of chloroprene in the presence of $AlCl_3$ (1 mole-%) under conditions described above there was obtained, after removing the unreacted starting materials, 19.76 g of the reaction product of which 3.61 g distilled at 80-110°/4 mm, leaving a residue (polymer) amounting to 15.32 g.

From the distilled portion there was obtained a substance boiling at 101-103°/4.5 mm, d^{20}_4 1.2082, $n^{20}D$ 1.5686.

Found %: Cl 49.32, ionizable Cl 16.994. M 208.4; bromine No. 149.2. $C_8H_{11}Cl_3$. Calculated %: Cl 49.88, ionizable Cl 16.63. M 213.5; bromine No. 149.7.

Examination of the polymers. To the solution of the polymers in benzene was added, portion-wise, methanol; the fractions obtained are described in the table below.

Physicochemical Constants of Polymer Fractions

Fraction No.	Weight		Mean molecular weight (cryosc., in benzene)		Total chlorine (%)		Ionizable chlorine (%)		Calculated empirical formula
	g	%	found	calc.	found	calc.	found	calc.	
1	6.68	27.31	662.3	656.0	42.57	43.29	6.33	5.26	$C_{28}H_{36}Cl_8$
2	12.58	52.82	458.2	479.0	43.22	44.46	7.75	7.41	$C_{20}H_{26}Cl_6$
3	4.87	19.87	257.3	—	—	—	—	—	Mixture of dimers and trimers

7.82 g of fraction 2 was submitted to ozonolysis. The products of decomposition were examined as before. The mixture of the acids contained no formic acid ($AgNO_3$ test). After distillation of the volatile acids in vacuo at 30-40° the residue contained 6.92 g of a mixture of chloroacetic and succinic acid (with a small amount of tarry matter).

Hydrochloric acid was determined from the chloride content of the mixture of the volatile acids; the determination gave 2.23 g (74.33%) of HCl.

The presence of acetic acid was confirmed by precipitation of its silver salt.

Found %: Ag 63.24. $C_2H_3O_2Ag$. Calculated %: Ag 64.59.

Silver salts of other acids could not be found. The amount of acetic acid was calculated from the total acidity of the mixed volatile acids which required 4.114 g of KOH for neutralization; of this 3.421 g was taken up by hydrochloric acid and 0.693 g by acetic acid, which corresponds to 0.743 g (77.57%) of acetic acid.

Chloroacetic acid was isolated from the crystalline residue by distillation in vacuo, m.p. 59-61°.

Found %: Cl 36.92. Acid value 596. $C_2H_3O_2Cl$. Calculated %: Cl 37.57. Acid value 597.

Total chlorine content of the crystalline product was found to be 0.462 g, which corresponds to 1.23 g (80.38%) of chloroacetic acid.

After recrystallization the melting point of the succinic acid was 179-181°.

Found: Acid value 939.5. $C_4H_6O_4$. Calculated: Acid value 949.18.

The aqueous extract required 9.2 g of KOH for neutralization of which 5.243 g was used up by hydrochloric, acetic and chloroacetic acids. Therefore, 5.35 g* KOH was taken up by the succinic acid, which corresponds to 5.92 g (74.44%) of the acid.

SUMMARY

1. Interaction of 1,3-dichlorobutene-2 with chloroprene in the presence of $FeCl_3$ and $AlCl_3$ as catalysts has been investigated.

2. It has been shown that in the presence of either catalyst 1,3-dichlorobutene-2 adds on to chloroprene in the 1,4-position, with the formation of products containing one, two, three and more molecules of chloroprene.

3. The product of the interaction of one molecule of 1,3-dichlorobutene-2 with one molecule of chloroprene has the structure of 1,3,7-trichlorooctadiene-2,6.

4. The polymers formed result from the condensation of one molecule of 1,3-dichlorobutene-2 and several chloroprene molecules by a step-wise addition to the primary reaction product (telomerization).

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Received March 5, 1957

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*As in original – Publisher's note.

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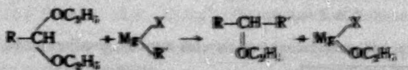
INVESTIGATION OF THE EXCHANGE OF OXY-RADICALS WITH HYDROCARBON RADICALS OF ORGANOMAGNESIUM COMPOUNDS

I. INVESTIGATION OF THE REACTIVITY OF MIXED ACETALS

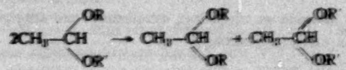
M. F. Shostakovskii and M. R. Kulibekov

In order to investigate the reactivity of oxy-radicals of mixed acetals of the general formula $CH_3-CH(OAlk)(OR)$, where $R = Alk$, Ar is an alkaryl radical, we have made use of the Chichibabin-Elgazin reaction [1]. As is well known, these authors have established that symmetrical acetals react with Grignard reagents according to the scheme



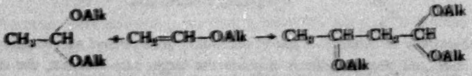
$$R-CH\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix} + Mg\begin{matrix}X\\R'\end{matrix} \rightarrow \underset{OC_2H_5}{R-CH-R'} + Mg\begin{matrix}X\\OC_2H_5\end{matrix}$$

In the present investigation Grignard reagents were used to establish the lability of oxy-radicals in mixed acetals, a facet which has not so far been reported on in the literature. As regards the reactivity of mixed acetals it is well known that under the influence of mineral acids or heat they easily undergo symmetrization



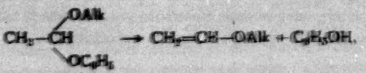
$$2CH_3-CH\begin{matrix}OR\\OR'\end{matrix} \rightarrow CH_3-CH\begin{matrix}OR\\OR\end{matrix} + CH_3-CH\begin{matrix}OR'\\OR'\end{matrix}$$

A characteristic reaction given by acetals, and one which demonstrates their high reactivity, is their interaction with simple vinyl ethers [2].



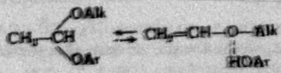
$$CH_3-CH\begin{matrix}OAlk\\OAlk\end{matrix} + CH_2{=}CH-OAlk \rightarrow CH_3-\underset{OAlk}{CH}-CH_2-CH\begin{matrix}OAlk\\OAlk\end{matrix}$$

As regards the structure of mixed acetals it has been established from results of their thermal decomposition [3] in accordance with the scheme



$$CH_3-CH\begin{matrix}OAlk\\OC_6H_5\end{matrix} \rightarrow CH_2{=}CH-OAlk + C_6H_5OH,$$

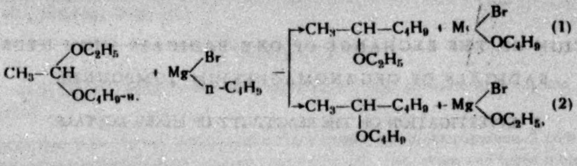
as also from investigation of their Raman spectra [4], that, for example, mixed alkaryl acetals may exist in the following two forms



$$CH_3-CH\begin{matrix}OAlk\\OAr\end{matrix} \rightleftarrows \underset{HOAr}{CH_2{=}CH-O-Alk}$$

In view of the fact that mixed acetals are assuming increasing theoretical and practical importance we have decided to investigate in detail the lability of their oxy-radicals by interaction with Grignard reagents. Three groups of mixed acetals were included in this investigation: (1) dialkyl, (2) alkyl-aryl and (3) alkyl-alkaryl acetals.

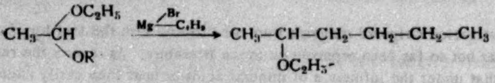
In the course of the investigation of the interaction of ethylbutyl acetal with butyl magnesium bromide it has been found that the reaction proceeds in two directions:


CH₃–CH(OC₂H₅)(OC₄H₉-n.) + Mg(Br)(n-C₄H₉)
→ CH₃–CH(OC₂H₅)–C₄H₉ + Mg(Br)(OC₄H₉) (1)
→ CH₃–CH(OC₄H₉)–C₄H₉ + Mg(Br)(OC₂H₅) (2)

of which reaction (1) is the predominant one.

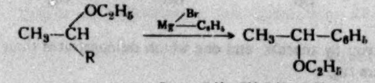
On acting on the same acetal with ethyl magnesium bromide it was found that neither the ethoxy nor the butoxy group undergoes substitution. Under the conditions of the reaction symmetrization of ethylbutyl acetal to the corresponding symmetrical acetals takes place. An analogous reaction with ethylbenzyl acetal also gave a negative result. Under the conditions of the reaction a portion of the ethylbenzyl acetal remains unchanged while a certain amount undergoes symmetrization with the formation of dibenzyl acetal. It may be concluded from this that under the conditions of the reaction ethyl bromide, unlike other alkyl (aryl) halides, favors symmetrization of mixed acetals.

On acting on ethylbenzyl and ethylphenyl acetals with butyl magnesium bromide, the ethyl ether of hexanol-2 is the sole product of the reaction.


CH₃–CH(OC₂H₅)(OR) —Mg(Br)C₄H₉→ CH₃–CH(OC₂H₅)–CH₂–CH₂–CH₂–CH₃

$R = CH_2C_6H_5,\ C_6H_5$

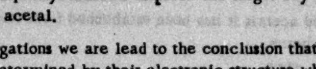
Action of phenyl magnesium bromide on ethylbutyl, ethylbenzyl and ethylphenyl acetals again gives one and the same ether as the main reaction product.



or $R = n\text{-}C_4H_9,\ CH_2C_6H_5,\ C_6H_5.$

The formation of ethylethers of hexanol-2 and of secondary phenylethyl alcohol shows unequivocally that in mixed acetals the butyl and phenyl radicals displace the larger oxy-radicals, the displacement being particularly easy with ethylphenyl acetal.

On the basis of these investigations we are lead to the conclusion that the lability for reactivity of given oxy-radicals of mixed acetals is determined by their electronic structure which facilitates the release of the OAr group in the form of an anion [5], with the formation of a carbonium ion;



The latter is easily stabilized either according to the scheme: $CH_3-C\overset{+}{H}-OAlk \to \overset{+}{H} + CH_2=CH-OAlk$ or the scheme $CH_3 \to \overset{+}{C}HOAlk + R \to \underset{\displaystyle R}{\underset{|}{CH_3}}CHOAlk$, where R = Alk, Ar or an alkaryl radical which determines the course of the exchange reaction.

EXPERIMENTAL

1. Interaction of ethylbutyl acetal with butyl magnesium bromide. Into a round-bottomed flask, provided with a stopcock, a mechanical stirrer, air-condenser and a dropping funnel, was placed 45 g of ethylbutyl acetal [b.p. 144-146° (735 mm), $n^{19}D$ 1.3995]. After heating up the contents on a boiling water bath an ether solution of butyl magnesium bromide, prepared in the usual way from 8 g of magnesium and 40 g of butyl bromide, was added slowly dropwise. As the reaction proceeded the solvent was gradually removed from the reacting system. When all of the organo-magnesium compound had been added heating was continued for 2-3 hours, the solvent being continuously removed. The reaction mixture was observed to heat up spontaneously (spontaneous boiling). At the end of the reaction time the reaction product was decomposed with water and 2-5% acetic acid. Whenever no unreacted organo-magnesium compound was present the decomposition with water proceeded slowly, without any excessive evolution of heat. The upper layer containing the required product was separated from the aqueous layer and was washed with 10% hydrochloric acid in order to hydrolize the unreacted acetal. The product obtained was then dissolved in ether, followed by washing with a weak sodium carbonate solution, and water, and was then dried over Na_2SO_4. The ether was removed on a water bath, the residue was fractionated at normal pressure.

The following fractions were collected:

Fraction 1- 101-123°, 1.5 g; fraction 2- 124-126°, 8 g, $n^{20}D$ 1.3964, d^{20}_4 0.7700, MR_D 40.60; Calculated 40.79; fraction 3-127-167°, 1 g; fraction 4-168-170°, 3 g, $n^{20}D$ 1.4098, d^{20}_4 0.7874, MR_D 50.13; Calculated 50.02. Residue 2 g.

The fraction boiling at 124-126° (747 mm) was identified as the ethyl ether of hexanol-2.

Found %: C 73.81; 73.94; H 13.80, 13.90. $C_8H_{18}O$. Calculated %: C 73.84; H 13.84.

The ethyl ether of hexanol-2 is a mobile clear colorless liquid having the odor of fruit. It is insoluble in water, but dissolves easily in organic solvents.

The fraction boiling at 168-170° (747 mm) was identified as the butyl ether of hexanol-2.

Found %: C 76.73, 73.68; H 14.00, 14.08. $C_{10}H_{22}O$. Calculated %: C 76.94; H 13.92.

The butyl ether of hexanol-2 is a colorless clear liquid with an aromatic odor. It is insoluble in water but dissolves easily in many organic solvents.

2. Interaction of ethylbutyl acetal with ethyl magnesium bromide. Under conditions similar to those used in the foregoing experiment ethyl magnesium bromide prepared from 6 g of magnesium and 27 g of ethyl bromide was added to 18 g of ethylbutyl acetal. Decomposition of the colorless reaction product with water was accompanied by vigorous fuming (after each drop of water) and spontaneous heating of the reaction mixture and for this reason the decomposition was conducted with external cooling. After suitable purification the product was distilled at atmospheric pressure.

The following fractions were collected: fraction 1, 99-179°, 2.5 g, $n^{21}D$ 1.4008; fraction 2, 179-181°, 4 g, $n^{21}D$ 1.4065. Residue 1.5 g.

Both fractions were combined and distilled again over metallic sodium. There was obtained 4 g of a liquid boiling at 182-183° (754.5 mm), $n^{20}D$ 1.4075, d^{20}_4 0.8277, which was identified as dibutyl acetal.

3. Interaction of ethylbutyl acetal with phenyl magnesium bromide. The preparation was carried out with 3 g of magnesium, 19 g of bromobenzene and 15 g of ethylbutyl acetal under conditions similar to those described in the foregoing experiments. The crude reaction product was of a dark brown color. No strong evolution of heat was observed during decomposition of the product with water. After suitable treatment the product was distilled in vacuo.

The following fractions were collected: fraction 1, 76-84° (10 mm), 3 g; fraction 2, 85-102° (10 mm), 5 g; residue 1 g.

Both fractions were combined and redistilled over metallic sodium. There was obtained 4.5 g of a liquid boiling at 120-122° (35 mm), $n^{20}D$ 1.4910, d^{20}_4 0.9203, which corresponds to the ethyl ether of sec. phenylethyl alcohol. Literature [6] gives a boiling point of 185-187°, d^{21} 0.931.

4. Interaction of ethylphenyl acetal with butyl magnesium bromide. Butyl magnesium bromide was prepared from 8 g of magnesium and 52 g of butyl bromide. Under conditions described above this reagent was added to 50 g of the acetal. After the addition of the first few drops a considerable amount of phenol separated and the reaction mixture turned into a solid black mass. The reaction product was extracted with ether and treated in the usual way. After removing the ether the residual mass became more and more viscous and finally changed into a dark-brown resin, resembling varnish rosin, which may have some practical application. The formation of the resin may be explained as being due to the decomposition of the acetal to vinylethyl ether and phenol under the action of the Grignard reagent under the given experimental conditions. The vinylethyl ether undergoes polymerization, the process being possibly catalyzed by the Grignard reagent. In order to prevent formation of the resin we changed the experimental conditions. To the prepared butyl magnesium bromide was added dropwise ethylphenyl acetal (without heating). After a short time the reaction mixture heated up spontaneously and came to the boil necessitating cooling with water. The product was decomposed with water without any marked evolution of heat. After the usual treatment the product was then distilled at atmospheric pressure.

The following fractions were collected: fraction 1, 80-126°, 2 g, n^{20}_D 1.3980, d^{20}_4 0.7927; fraction 2, 127-130°, 6 g, n^{20}_D 1.3970, d^{20}_4 0.7732; fraction 3, 131-132°, 5 g, n^{20}_D 1.3976; d^{20}_4 0.7730. Residue 1.5 g.

Fractions 2 and 3 were combined and redistilled over metallic sodium yielding 8 g of the ethyl ether of hexanol-2; b.p. 126-128° (741.5 mm), n^{20}_D 1.3952, d^{20}_4 0.7670, MR_D 40.65; Calculated 40.79.

5. Interaction of ethylphenyl acetal with phenyl magnesium bromide. To phenyl magnesium bromide prepared from 3 g of magnesium and 19 g of bromobenzene was added, dropwise, 16 g of the acetal [b.p. 87.5-88.5° (11 mm), n^{19}_D 1.4972]. The synthesis was carried out under the same conditions as those described above. The reaction product was distilled in vacuo. The fraction boiling at 75-76° (12 mm) was collected (10.7 g). In the later stages of the distillation phenol crystallized in the condenser. The fraction boiling at 75-76° (12 mm) was redistilled twice over metallic sodium. There was obtained 5 g of a liquid boiling at 70.5° (12 mm), n^{20}_D 1.4930, d^{20}_4 0.9220, MR_D 47.28; Calculated 46.42.

This liquid was identified as the ethyl ether of sec. phenylethyl alcohol. Its structure was proved by synthesis of the analogous acetal from ethylbutyl acetal and phenyl magnesium bromide (Experiment No. 3).

6. Interaction of ethylbenzyl acetal with ethyl magnesium bromide. Ethyl magnesium bromide was prepared from 6 g of magnesium turnings and 27 g of ethylbromide. The reagent was added from a dropping funnel to 32 g of ethylbenzyl acetal, as in Experiment No. 1. On decomposing the product with water there was copious evolution of fumes and spontaneous heating of the reaction mixture. The product was distilled over metallic sodium.

Fractions collected: Fraction 1, b.p. 102-103° (10 mm), 7 g, n^{19}_D 1.4878; d^{19}_4 0.9777; fraction 2, 182-183° (10 mm), 7 g, n^{19}_D 1.5388, d^{19}_4 0.0491. Residue 1.5 g.

Fraction No. 1 was found to be ethylbenzyl acetal and fraction 2 was identified as dibenzyl acetal; this result indicates that no symmetrization takes place. On the other hand ethylbenzyl acetal undergoes symmetrization under the action of ethyl magnesium bromide.

The ethylbenzyl acetal used in this synthesis was first prepared by us in 70% yield by the method described previously [8].

B.p. 219-220°, n^{20}_D 1.4861, d^{20}_4 0.9783, MR_D 52.83; Calculated 52.68.

Found %: C 73.70, 73.70; H 8.88, 8.94. $C_{11}H_{16}O_2$. Calculated %: C 73.33; H 8.88.

Ethylbenzyl acetal is a clear colorless liquid with a light odor of ether. It is insoluble in water.

7. Interaction of ethylbenzyl acetal with butyl magnesium bromide. The preparation was carried out with 6 g of magnesium, 34 g of butyl bromide and 40 g of the acetal under the same conditions as in Experiment No. 1. The reaction product was distilled at atmospheric pressure.

Obtained: fraction 1, b.p. 102-122°, 0.5 g; fraction 2, 123-126°, 2.5 g; fraction 3, 127-129°, 4 g. Residue 7 g.

Fractions 2 and 3 were combined and redistilled over metallic sodium. There was obtained 3.5 g of the ethyl ether of hexanol-2, b.p. 129-130.5° (754 mm), n^{20}_D 1.3990, d^{20}_4 0.7681. The 7 g of the residue was identified as a benzyl alcohol. The structure of the product follows from the synthesis described in the foregoing experiments (Experiment Nos. 1, 4, 7).

8. Interaction of ethylbenzyl acetal with phenyl magnesium bromide. The preparation was carried out with 1/8 mole of each reagent, the conditions being similar to those in Experiment No. 1. The resultant product was distilled in vacuo, yielding 5.5 g of a liquid [b.p. 75-77° (14 mm), $n^{20}D$ 1.4945, d^{20}_4 0.9233], which was identified as the ethyl ether of sec. phenylethyl alcohol [6].

9. Interaction of butyl benzyl acetal with phenyl magnesium bromide. The Grignard reagent was prepared from 8 g of magnesium and 50 g of bromobenzene. It was added to 55 g of butylbenzyl acetal preheated on a water bath. The reaction product was fractionated in vacuo.

Fractions obtained: Fraction 1, 92.5-93.5° (13 mm), 9 g, $n^{20}D$ 1.5040, d^{20}_4 0.9626; fraction 2, 94-99° (13 mm), 5 g, $n^{20}D$ 1.4930, d^{20}_4 0.9333. Residue 2 g.

The two fractions were combined and treated with metallic sodium. A vigorous reaction took place with the formation of a fluffy precipitate. The reaction product was separated from the precipitate by filtration and distilled over metallic sodium. The following fractions were collected: Fraction 1, 214-218° (758 mm), 2 g, $n^{20}D$ 1.4862, d^{20}_4 0.9133; fraction 2, 219-220° (758 mm), 3.5 g, $n^{20}D$ 1.4848, d^{20}_4 0.9105.

The fraction boiling at 219-220.5° (758 mm), was identified as the butyl ether of sec. phenylethyl alcohol. Literature [7] gives a boiling point of 220-222° (730 mm), d^{20}_4 0.9063, $n^{20}D$ 0.4832.

The butylbenzyl acetal used in this preparation was first obtained by us in approximately 75% yield by the method described previously [8]. The acetal has the following characteristics:

B.p. 142.5° (18 mm), d^{20}_4 0.9530, $n^{20}D$ 1.4794, MR_D 61.59; Calculated 61.92.

Found %: C 74.70, 74.59; H 9.44, 9.28. $C_{13}H_{20}O_2$. Calculated %: C 75.00; H 9.61.

Butylbenzyl acetal is a clear colorless liquid with a faint odor of ether. It is insoluble in water but dissolves easily in many organic solvents.

SUMMARY

1. The exchange of oxy-radicals of mixed acetals for alkyl and aryl radicals of Grignard reagents has been investigated.

2. It has been shown that it is the heavier oxy-radicals which undergo displacement.

3. The synthesis of the ethyl and the butyl ethers of hexanol-2, ethylbenzyl acetal and butylbenzyl acetal has been described for the first time.

The high reactivity of alkyl-aryl acetals has been demonstrated.

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Received February 18, 1957

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* Original Russian pagination. See C.B. Translation.

ELECTRON CHARGE DENSITY OF CHEMICAL BONDS AND THE CHEMICAL PROPERTIES OF MOLECULES

I. ENERGIES OF ACTIVATION OF SUBSTITUTION REACTIONS AT A SATURATED CARBON ATOM

G. V. Bykov

In earlier papers we have shown [1-3] that the magnitude of the electron charge density of a covalent bond determines its more important physical characteristics and its behavior in chemical reactions. There is thus opened the possibility of a broad interpretation of chemical properties of complex molecules based, firstly, on the introduction of a new structural factor, namely, the electron charge density of the bond, and, secondly, on the fact that the regularities observed in chemical properties follow from the already established relationships between electron charge densities and energy parameters of molecules and individual bonds. A particular feature of the treatment of the problem outlined here is its semiquantitative character; however, in order to deduce qualitative relationships relating to the reactivity of molecules it is sufficient to know not the absolute, but merely the relative values of electronic charges of the bonds involved. The author has already put forward and exemplified [3] the following hypothesis: the energy of activation and hence, also the rate of substitution at a given bond are related to its electron charge density. In the present communication we shall apply this hypothesis to substitution reactions at a saturated carbon atom by different mechanisms. Corresponding reactions with unsaturated and aromatic compounds will be dealt with later. The discussion which follows will therefore apply to σ-electron bond charges only.

Electrophilic (a), radical (b) and nucleophilic (c) substitution reactions following a unimolecular mechanism may be represented by the following schemes:

$$\begin{array}{lll} \mathrm{R}-|\mathrm{X} \rightarrow \mathrm{R}^- + \mathrm{X}^+ & \text{followed by} & \mathrm{R}^- + \mathrm{Y}^+ \rightarrow \mathrm{R}-\mathrm{Y}\ (a) \\ \mathrm{R} \nmid \mathrm{X} \rightarrow \mathrm{R}\cdot + \mathrm{X}\cdot & \text{followed by} & \mathrm{R}\cdot + \mathrm{Y}\cdot \rightarrow \mathrm{R}-\mathrm{Y}\ (b) \\ \mathrm{R}|-\mathrm{X} \rightarrow \mathrm{R}^+ + \mathrm{X}^- & \text{followed by} & \mathrm{R}^+ + \mathrm{Y}^- \rightarrow \mathrm{R}-\mathrm{Y}\ (c) \end{array}$$

The rate of these reactions is determined by the rate of the slowest step — the breakdown of the molecule R — X into R and X. It is evident that the energy of activation of this step will be less, and the rate of reaction greater,* in case (a) the smaller the electron charge of the R — X bond. The same holds true in case (c) the greater the charge of the R — X bond. Less clear is the situation in case (b), but since the energies of radical dissociation of bonds are, in general, symbatic to the "mean" bond energies which, in turn, are proportional to the bond electron charges [1], it may be assumed that the energy of activation of the radical substitution reaction will be less the smaller the electron charge density of the corresponding bond. As will be seen later, this assumption does, in fact, correspond to reality.

When the above-mentioned reactions proceed according to the bimolecular mechanism they involve the formation of the intermediate complex $\mathrm{Y}\ldots\ldots\overset{|}{\underset{\wedge}{\mathrm{C}}}\ldots\ldots\mathrm{X}$. The energy of activation of such reactions is made up mainly of two components: the energy of repulsion between Y and the carbon atom together with the original atoms attached to it, and the energy required to stretch the C – X bond, which, in turn, depends on the electron charge density of this bond. If in a series of different molecules the carbon atoms at which substitution is to take place do not differ to any great extent with respect to electronegative character from the atoms attached to them, then the differences in the energies of activation between the individual reactions will be mainly due to differences in the electron charge density of the C – X bonds in the various molecules. What has been said above with regard to the role of the electron charge density in substitution reactions by the unimolecular mechanism applies again in this case.

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* In comparing different reactions involving similar reagents, reaction mechanisms and experimental conditions, we may neglect the changes (as we pass from one reaction to another) in the pre-exponential term in Arrhenius' equation and compare only the energies of activation of the reactions or the rate constants which are simply related to the former.

We shall now carry out a comparison of the energies of activation of substitution reactions with the electron charge densities of the corresponding bonds. A simple formula has been proposed [1,4] for calculating the electron charge density of a bond, A_{CX}:

$$A_{CX} = 1 + \frac{4E_X}{\Sigma E},$$

where E_X is the electronegativity of the monovalent atom X and ΣE the sum of electronegativities of all the atoms attached to the carbon atom forming the C – X bond. In applying this formula we shall make use of the electronegativity scale referred to hydrogen, as put forward by B. V. Nekrasov [5]:

H	Li	C	Cl	Br	I
1.00	0.40	1.19	1.43	1.37	1.24

The substitution of lithium by hydrogen in organolithium compounds is a characteristic example of electrophilic substitution. In the formation of the lithium derivative of dibenzofuran:

$$R - |Li + C_{12}H_8O \rightarrow R - H + C_{12}H_7LiO$$

the ease of demetalation of lithium alkyls decreases [6] and, consequently, the energy of activation, ε, of the metallation reaction increases in the series:

$$\begin{array}{lclclcl} (CH_3)_3CLi & < & CH_3CHLiCH_2CH_3 & < & CH_3CH_2CH_2CH_2Li & < & CH_3Li \\ A_{CLi} = 1.40 & & 1.42 & & 1.45 & & 1.47 \text{ electrons} \end{array}$$

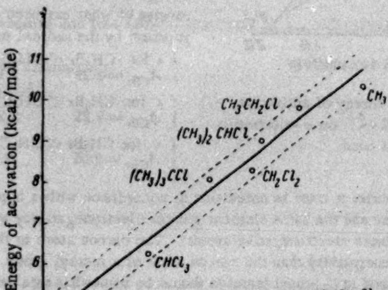

Fig. 1. Dependence of the energy of activation of the reaction $Na\cdot + RCl \rightarrow NaCl + R\cdot$ [8,9] on σ-electron charge density of the C – Cl bond.

a feature which runs parallel to the increasing σ-electron charge of the C – Li bonds. The inequality signs in this case again refer to the energies of activation of the corresponding reactions.

In radical substitution, for example in the case of the nitration of unsaturated hydrocarbons, the ease of substitution of hydrogen becomes less and the energy of activation, ϵ, greater in the series:

$$\begin{array}{llll} & R_3CH < & R_2CH_2 < & RCH_3 \\ A_{CH} = & 1.88 & 1.91 & 1.95 \text{ electrons} \end{array}$$

M. B. Neiman and co-workers [7] have found that in isotope exchange reactions $R\dot{I} + I\cdot \rightarrow RI + \dot{I}\cdot$, which take place in cyclohexane solutions of active alkyl iodide and inactive free iodine (which gives rise to the formation of atomic iodine under the influence of light) the following relationship between the energies of activation holds:

$$\left\{\begin{array}{llll} \epsilon \text{ for} & CHI_3 < & CH_2I_2 < & CH_3I \\ A_{CI} = & 2.05 & 2.11 & 2.17 \text{ electrons} \end{array}\right.$$

$$\left\{\begin{array}{llll} \epsilon \text{ for} & (CH_3)_2CHI < & CH_3CH_2I < & CH_3I \\ A_{CI} = & 2.07 & 2.12 & 2.17 \text{ electrons} \end{array}\right.$$

We thus find that there is a definite parallelism between the decrease in the rate of reaction, the increase in the energy of activation of the reaction, and the increase in the electron charge density of the bond involved in a substitution reaction by the radical mechanism. From Fig. 1 it will be seen that there is a linear relationship between the energies of activation of the reaction $Na\cdot + RCl \rightarrow NaCl + R\cdot$ and the electron charge density of the C – Cl bond being ruptured. At any rate, all the points, with the exception of one, come to lie within a band bounded by two parallel broken lines which correspond to the limits of error in the determination of the energy of activation of the reaction in question, namely, ± 0.5 kcal/mole (according to Semenov [8] the limits of error in such determinations are, at best, ±0.5-1.0 kcal/mole). The point representing the case of allyl chloride lies well outside this band; however, the problem of the special features of the "allylic position" of the substituent belongs to the class of unsaturated compounds which is not being touched upon here.

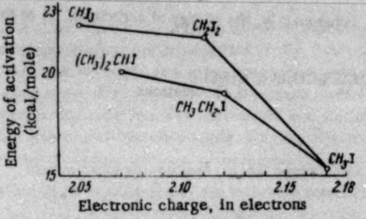

Fig. 2. Dependence of the energy of activation of the reaction $R\dot{I} + I \rightarrow RI + \dot{I}^-$ on σ-electronic charged density of the C – I bond.

Neiman and co-workers have also investigated [7] the nucleophilic substitution-reactions $RX + \dot{X} \rightarrow R\dot{X} + X^-$, where X = Br or I. They effected the interaction between the inactive alkyl halide and an active sodium halide, in solution in aqueous alcohol. It is found that the relationship between the rate of reaction and the energy of activation, on the one hand, and the electron charge densities of the C – X bonds, on the other, is the reverse of what has been observed in the case of substitution by the radical mechanism. Thus,

$$\left\{\begin{array}{llll} \epsilon \text{ for} & CH_3Br < & CH_2Br_2 < & CHBr_3 \\ A_{CBr} = & 2.25 & 2.16 & 2.07 \text{ electrons} \end{array}\right.$$

$$\left\{\begin{array}{llll} \epsilon \text{ for} & CH_3Br < & CH_3CH_2Br < & (CH_3)_2CHBr \\ A_{CBr} = & 2.25 & 2.20 & 2.15 \text{ electrons} \end{array}\right.$$

$$\left\{\begin{array}{llll} \epsilon \text{ for} & CH_3Br < & CH_3CH_2Br < & CH_3CH_2CH_2Br \\ A_{CBr} = & 2.25 & 2.20 & \text{less than } 2.20 \text{ electrons} \end{array}\right.$$

With regard to the last series it must be noted that in accordance with a hypothesis formulated earlier [1] (i.e. of several atoms of one and the same element greater electronegativity will be exhibited by that atom which is directly attached to more electronegative atoms). The carbon atom in the methylene group should exhibit somewhat greater electronegativity than the carbon atom of a methyl group, and consequently, the electron charge density of the C – Br bond in n-propyl bromide should be somewhat smaller than in ethyl bromide. From this it follows that in nucleophilic substitution reactions ethyl bromide should be more active than n-propyl bromide.

The comparison of energies of activation determined by Neiman for reactions involving nucleophilic substitution reactions with alkyl iodides is illustrated graphically in Fig. 2. For similar values of electron charge densities of the C – I bonds the energies of activation are smaller for those derivatives of methyl iodide which have been obtained by substituting its hydrogen atoms by methyl groups, whereas they are greater when these atoms are substituted by further iodine atoms. This result is explained by the fact that in the latter case the component of the energy of activation necessary to overcome the force of repulsion between the entering substituent and the group of atoms surrounding the carbon atom to be substituted is greater in the latter case (cf. [3]).

The examples of substitution reactions at a saturated carbon atom considered here are, of course, relatively simple since here we have to take into account only the distribution of σ-electron charges in the molecule. However, even in cases of substitution in the "allylic position" the distribution of the π-electronic cloud among the bonds of the molecule begins to exert an influence on the energy of activation of such reactions. Only when methods are developed which permit the calculation, or even a rough estimation, of the distribution of electron charge densities in unsaturated compounds, including aromatic ones, will be possible to investigate the dependence of the energy of activation of reactions on the distribution not only of σ-, but also of π-electronic charges.

SUMMARY

1. The energy of activation of electrophilic and radical substitution reactions at a saturated carbon atom increases with increasing σ-electronic charge density of the bond involved in the substitution.

2. The reverse type of dependence governs nucleophilic substitution.

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Received February 25, 1957

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*Original Russian pagination. See C.B. Translation.

**In Russian.

DOUBLE DIAZONIUM SALTS OF METHYLTIN TRICHLORIDE AND DIETHYLTIN DICHLORIDE

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The well-known double diazonium salts of tin tetrachloride have first been synthesised by Griess [1] and have later been investigated in detail by Kocheshkov and Nesmeianov [2]. These salts are the starting materials in the preparation of organotin compounds by the diazo method developed by Nesmeianov [3]. As regards double diazonium salts of organotin compounds, these have so far been unknown. The present paper describes the preparation of double diazonium salts of methyltin trichloride and diethyltin dichloride.

One of us [4] has developed a method for the synthesis of double diazonium salts of organoantimony compounds based on an exchange reaction between the double diazonium salt of ferrous chloride and the given organoantimony compound. This method was also found applicable in the preparation of double diazonium salts of methyltin trichloride. These salts were precipitated on mixing, in the cold, in an acetone solution of the freshly prepared diazonium salt* $ArN_2Cl \cdot FeCl_3$ with a methanolic solution of CH_3SnOOH saturated with hydrogen chloride. The reactions which take place may be expressed by the following equations.

$$CH_3SnOOH + 3HCl \rightarrow CH_3SnCl_3 + 2H_2O,$$

$$2ArN_2Cl \cdot FeCl_3 + CH_3SnCl_3 \rightarrow (ArN_2Cl)_2 \cdot CH_3SnCl_3 + 2FeCl_3.$$

The salts $(C_6H_5N_2Cl)_2 \cdot CH_3SnCl_3$ and $(p\text{-}C_7H_7N_2Cl)_2 \cdot CH_3SnCl_3$ could not be prepared by this method since on mixing the solutions in the cold vigorous evolution of nitrogen took place. The double salts $(p\text{-}O_2NC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$ and $(m\text{-}O_2NC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$ were precipitated only in traces, evidently because of their good solubility.

Subsequently we have worked out a simpler single-step method of synthesis of double diazonium salts of methyltin trichloride.** A solution of CH_3SnOOH in hydrochloric acid was added to the diazonium solution prepared by diazotizing the aromatic amine in hydrochloric acid with solid sodium nitrite; a precipitate of the salt $(ArN_2Cl)_2 \cdot CH_3SnCl_3$ formed at once. When it was attempted to prepare in this way the double salt using o-toluidine there was evolution of nitrogen and the salt did not precipitate. The double salts formed with $p\text{-}O_2NC_6H_4N_2Cl$ and $p\text{-}CH_3COC_6H_4N_2Cl$ did not precipitate probably because of their solubility in hydrochloric acid. It must be noted that the double salt does form with phenyl diazonium chloride, but in spite of many attempts could not be obtained in the pure state. Double diazonium salts of methyltin trichloride prepared by both methods are listed in Table 1.

The single-step method of preparation of double diazonium salts in hydrochloric acid solution which was found best for the purpose of the synthesis of salts of the type $(ArN_2Cl)_2 \cdot CH_3SnCl_3$, could not be applied to the preparation of double diazonium salts of diethyltin dichloride in view of the poor solubility of the latter in hydrochloric acid. On the other hand, on mixing the hydrochloric acid solution of the aryldiazonium chloride with an alcoholic solution of diethyltin dichloride gives rise to the co-precipitation of sodium nitrite which is formed during diazotization. For this reason we have adopted the following method to prepare double

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*Double diazonium salts of ferrous chloride were prepared by the method described in [2].

**Double diazonium salts with $p\text{-}BrC_6H_4N_2Cl$ and $C_6H_5N_2Cl$ were also prepared by mixing an alcoholic solution of ArN_2Cl with an alcoholic solution of CH_3SnOOH saturated with hydrogen chloride.

TABLE 1

Double diazonium salt	Melting point (decomp)	Yield (%)	
		Method I	Method II
$(p\text{-}CH_3C_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$	112°	34.0	34.0
$(p\text{-}CH_3OC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$	165	32.5	42.0
$(p\text{-}BrC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$	147	—	42.5
$(p\text{-}C_2H_5OCOC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$	108	25.0	25.0
$(o\text{-}O_2NC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$	106	—	43.7

diazonium salts of $(C_2H_5)_2SnCl_2$:[**] the amine hydrochloride was dissolved in alcohol and diazotized with isoamyl nitrite and to the diazo solution was then added an alcoholic solution of diethyltin dichloride. The formation of the double salt of $(C_2H_5)_2SnCl_2$ may be expressed by the following equations:

$$ArNH_2 \cdot HCl + C_5H_{11}ONO \rightarrow ArN_2Cl + C_5H_{11}OH + H_2O,$$
$$2ArN_2Cl + (C_2H_5)_2SnCl_2 \rightarrow (ArN_2Cl)_2 \cdot (C_2H_5)_2SnCl_2.$$

The salts prepared by this method are listed in Table 2. Attempts to synthesise by this method the double diazonium salts starting from $p\text{-}O_2NC_6H_4NH_2$ and $p\text{-}CH_3COC_6H_4NH_2$ were unsuccessful because of the good solubility of these salts in alcohol.

TABLE 2

Double diazonium salts	Melting point (decomp.)	Yield (%)
$(C_6H_5N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$	80—81°	94
$(p\text{-}CH_3C_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$	88—89	74
$(p\text{-}ClC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$	98—99	83
$(p\text{-}BrC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$	110	68
$(p\text{-}C_2H_5OCOC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$	80	85

Double diazonium salts of methyltin trichloride and diethyltin dichloride have, as have the corresponding salts of $SnCl_4$, a constant composition $[ArN_2]_2^{+}[CH_3SnCl_5]^{--}$ or $[ArN_2]_2^{+}[(C_2H_5)_2SnCl_4]^{--}$ which is independent of the amounts of reagents used or of the character of the aryl radicals of the diazonium compound. Salts of both types are colorless crystalline compounds which undergo change on exposure to light, are easily soluble in water, less soluble in alcohol, and insoluble in ether, acetone and benzene.

EXPERIMENTAL

Preparation of double diazonium salts of CH_3SnCl_3 by mixing hydrochloric acid solutions of ArN_2Cl and CH_3SnCl_3. 1. 1.93 g (0.018 mole) of $p\text{-}CH_3C_6H_4NH_2$ was diazotized with 1.2 g (0.018 mole) of $NaNO_2$ in a mixture of 5.4 ml of conc. HCl and 5.4 g of ice. To the diazo solution was added a cold solution of 1.5 g (0.009 mole) of CH_3SnOOH in 10 ml of conc. HCl. The precipitated double salt was filtered off and purified by reprecipitation from methanol with ether. Yield 1.6 g (34%). M.p. 112° (decomp.)

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[*] Preparation of the double salts $(ArN_2Cl)_2 \cdot CH_3SnCl_3$ by method I involved the formation of double diazonium salts of ferrous chloride; preparation by method II was by mixing solutions of ArN_2Cl in hydrochloric acid with CH_3SnOOH.

[**] The reaction between $ArN_2Cl \cdot FeCl_3$ with diethyltin dichloride to yield double diazonium salts of diethyltin dichloride was not investigated.

Found %: N 10.35, 10.19; Sn 21.72, 21.97.* $(C_7H_7N_2Cl)_2 \cdot CH_3SnCl_3$. Calculated %: N 10.20; Sn 21.61.

2. From 2.2 g (0.018 mole) of p-$CH_3OC_6H_4NH_2$ and 1.5 g (0.009 mole) of CH_3SnOOH there was obtained, under conditions described in the foregoing experiment, 2.2 g (42%) of the corresponding double diazonium salt. M.p. 164-165° (decomp.).

Found %: N 9.13, 9.15. $(CH_3OC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. Calculated %: N 9.63

3. From 3.1 g (0.018 mole) of p-$BrC_6H_4NH_2$ and 1.5 g (0.009 mole) of CH_3SnOOH was obtained 2.6 g (42.2%) of the double diazonium salt under the usual conditions; M.p. 147° (decomp.).

Found %: N 8.70, 8.89; Sn 17.99, 17.65 (p-$BrC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. Calculated %: N 8.89; Sn 17.48.

4. From 3 g (0.018 mole) of p-$C_2H_5OCOC_6H_4NH_2$ and 1.5 g (0.009 mole) of CH_3SnOOH there was obtained 1.5 g (25%) of the double diazonium salt; M.p. 108° (decomp.).

Found %: Sn 17.72, 17.78. $(C_2H_5OCOC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. Calculated %: Sn 17.84.

5. From 2.5 g (0.018 mole) of o-$O_2NC_6H_4NH_2$ and 1.5 g (0.009 mole) of CH_3SnOOH there was obtained 2.4 g (43.7%) of the diazonium salt in the usual way. M.p. 106° (decomp.).

Found %: Sn 19.50, 19.08. $(O_2NC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. Calculated %: Sn 19.42.

Preparation of double diazonium salts of methyltin trichloride through the double diazonium salts of ferrous chloride. 1. To a solution of 3.5 g (0.018 mole) of p-$CH_3C_6H_4N_2Cl \cdot FeCl_3$ in the minimum amount of acetone was added in the cold a solution of 1.5 g (0.009 mole) of CH_3SnOOH in 17 ml of methanol saturated with hydrogen chloride. The precipitate of the double salt (p-$C_7H_7N_2Cl)_2 \cdot CH_3SnCl_3$ was filtered off and purified by reprecipitation with ether from methanol. Yield 1.7 g (34%), m.p. 112° (decomp.). An authentic sample of a double salt of this composition melts at 112° (decomp.).

2. From 6 g (0.018 mole) of p-$CH_3OC_6H_4N_2Cl \cdot FeCl_3$ and 1.5 g (0.009 mole) of CH_3SnOOH there was obtained, under conditions used in the foregoing experiment, 1.7 g (32.5%) of (p-$CH_3OC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. M.p. 165° (decomp.). An authentic sample of the double salt of p-anisyldiazonium chloride and methyltin trichloride melts at 165° (decomp.).

3. From 6.8 g (0.018 mole) of p-$C_2H_5OCOC_6H_4N_2Cl \cdot FeCl_3$ and 1.5 g (0.009 mole) of CH_3SnOOH was obtained, under the usual conditions, 1.4 g (25%) of (p-$C_2H_5OCOC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$. M.p. 108° (decomp.). An authentic sample of this salt melts at 108° (decomp.).

Preparation of double salts of p-bromophenyldiazonium chloride and methyltin trichloride. 3.1 g (0.018 mole) of p-bromoaniline hydrochloride was dissolved in 15 ml of alcohol. To this solution was added 0.5 ml of alcoholic HCl followed by the gradual addition of 2.7 g (0.018 mole) of isoamyl nitrite with cooling in ice. The diazonium chloride solution was allowed to stand for 15 minutes after which a solution of 1.5 g of CH_3SnOOH (0.009 mole) in 17 ml of alcoholic HCl was added. The salt which precipitated was filtered off and purified by reprecipitation with ether from methanol. Yield 2.5 g (42%), m.p. 147° (decomp.). The authentic salt having the structure (p-$BrC_6H_4N_2Cl)_2 \cdot CH_3SnCl_3$ melts at 147° (decomp.).

Preparation of double diazonium salts of diethyltin dichloride. 1. To a solution of 1.1 g (0.008 mole) of aniline hydrochloride in 7.5 ml of alcohol was added 0.5 ml of alcoholic HCl and 0.94 g (0.008 mole) of isoamyl nitrite with cooling. To this diazo solution was added a solution of 1 g (0.004 mole) of $(C_2H_5)_2SnCl_2$ in 1 ml of alcohol. The precipitate of the double salt of phenyl diazonium chloride and diethyltin dichloride was filtered off and reprecipitated with ether from alcohol. Yield 2 g (94%), m.p. 80-81° (decomp.).

Found %: Sn 22.24, 22.22. $(C_6H_5N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$. Calculated %: Sn 22.45.

2. From 1.32 g (0.008 mole) of p-$ClC_6H_4NH_2 \cdot HCl$, dissolved in 5 ml of alcohol, and 1 g (0.004 mole) of $(C_2H_5)_2SnCl_2$ there was obtained 2 g (83%of the corresponding double diazonium salt. M.p. 98-99° (decomp.).

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* Because of unsatisfactory results obtained with the usual method of analysis of organotin compounds for tin [5] when applied to double diazonium salts, the method has been modified somewhat. The decomposition of the salt was initiated in a quartz test tube by heating 0.5 g of the compound with 2-3 drops of water. To complete the decomposition a mixture of HNO_3 and H_2SO_4 (about 30 drops) was then added. The analysis was then continued in the usual way.

Found %: Sn 19.32, 19.63. $(ClC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$. Calculated %: Sn 19.86.

3. From 1.66 g (0.008 mole) of p-$BrC_6H_4NH_2 \cdot HCl$, dissolved in the minimum amount of alcohol, and 1 g (0.004 mole) of diethyltin dichloride there was obtained under the usual conditions, 1.85 g (68%) of the corresponding double salt. M. p. 110° (decomp.).

Found %: Sn 17.29, 16.89. $(BrC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$. Calculated %: Sn 17.29.

4. From 1.62 g (0.008 mole) of p-$C_2H_5OCOC_6H_4NH_2 \cdot HCl$, dissolved in 3.5 ml of alcohol and 1 g (0.004 mole) of $(C_2H_5)_2SnCl_2$ there was obtained, under the usual conditions, 2.3 g (85%) of the double salt. M.p. 80° (decomp.).

Found %: Sn 17.47, 17.30. (p-$C_2H_5OCOC_6H_4N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$. Calculated %: Sn 17.64.

5. From 1.2 g (0.008 mole) of p-$CH_3C_6H_4NH_2 \cdot HCl$, dissolved in the minimum amount of alcohol, and 1 g (0.004 mole) of $(C_2H_5)_2SnCl_2$ there was obtained, under the usual conditions, 1.6 g (74%) of the double salt. M.p. 88-89° (decomp.).

Found %: Sn 21.90. $(C_7H_7N_2Cl)_2 \cdot (C_2H_5)_2SnCl_2$. Calculated %: Sn 22.40.

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Received February 7, 1957

INVESTIGATION OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

XX. REACTION OF ETHYL ESTERS OF β-NITROPHENYLGLYCIDIC ACIDS AND p-CHLOROPHENYLGLYCIDIC ACID WITH AMMONIA AND ANILINE

V. F. Martynov and G. Ol'man

In one of our recent studies [1] we investigated the reaction of ethyl esters of β-phenylglycidic acids containing electron-donor substituents in the phenyl ring with ammonia and aromatic amines. In this work it was established that all phenylglycidic esters with electron-donor groups add amines in the same way as unsubstituted phenylglycidic esters, i.e., in the α-position. For a final resolution of the question of the effect of a substituent in the phenyl ring of glycidic acids on the place of opening of the oxide ring under the influence of amines it was necessary to investigate the β-phenylglycidic esters containing electron-accepting substituents in the phenyl ring. For this purpose we synthesized and investigated the ethyl esters of β-(p-nitrophenyl)-, β-(m-nitrophenyl)-, β-(o-nitrophenyl)-, and β-(p-chlorophenyl) glycidic acid.

All our attempts to add aniline and ammonia to the ethyl ester of β-(o-nitrophenyl) glycidic acid were unsuccessful. In the literature it is indicated [2] that this reaction is easily accomplished by the action of aniline with the sodium salt of β-(o-nitrophenyl) glycidic acid. We repeated the experiments of these authors and actually obtained the same product to which they ascribed the formula α-hydroxy-β-anilino-β-(o-nitrophenyl) propionic acid. However, the compound indicated split out aniline with extreme ease upon heating with barium hydroxide, which is characteristic only of aniline salts. In this connection we carried out a spectroscopic study in the infrared both of β-(o-nitrophenyl) glycidic acid itself and of its reaction product with aniline. In this study it appeared that the characteristic frequency for the oxide ring also was evident in the latter (Fig. 1). Consequently, in this case also addition of aniline to the oxide ring did not take place, and the product formed was the corresponding aniline salt.

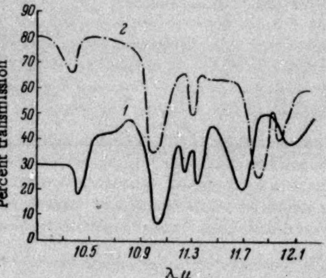
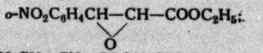
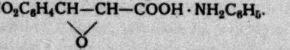
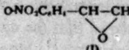
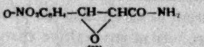
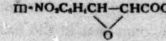
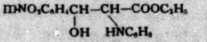
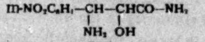
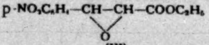
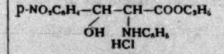
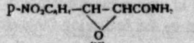
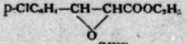
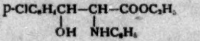
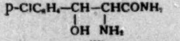


Fig. 1. 1 —

$o\text{-}NO_2C_6H_4CH\text{—}CH\text{—}COOC_2H_5$;

2—

$o\text{-}NO_2C_6H_4CH\text{—}CH\text{—}COOH \cdot NH_2C_6H_5$.

The ethyl ester of β-(p-nitrophenyl) glycidic acid gave an addition product with aniline, although in small yield. With regard to the ethyl ester of β-(m-nitrophenyl) glycidic acid, the corresponding aniline addition product was obtained in 57% yield. The isolation of the reaction products in these two instances was very difficult. Purification by distillation was impossible because the boiling point was too high and explosive decomposition was possible. Precipitation (as the hydrochlorides) in anhydrous alcohol solution by passing gaseous hydrogen chloride through did not give positive results either, and only the use of concentrated hydrochloric acid, which was added to an alcohol solution of the reaction product previously freed of excess aniline, gave the desired result. On prolonged standing, the reaction products with aniline separated out as hydrochlorides. For the ethyl ester of β-(p-chlorophenyl) glycidic acid the reaction with aniline proceeded rather easily and the addition product was obtained in good yield (60%).

The determination of the structure of the compounds mentioned was carried out by noting their behavior with concentrated sulfuric acid. If aniline added to the β-carbon atom, according to the general scheme found by us for the transformation of such compounds, then carbon monoxide should be evolved and the corresponding 2-phenylindole should form [3]. However, formation of the indoles was not observed for any of the aniline addition products obtained. On this basis it could be assumed with complete certainty that opening of the oxide ring in the glycidic acids investigated took place at the α-carbon atom and consequently we obtained the α-amino-β-hydroxy acids. The formulas of the compounds obtained are given in the table.

Ethyl ester of glycidic acid	Reaction product	
	with aniline	with ammonia
 (I)	—	 (II)
 (V)	 $m\text{-}NO_2C_6H_4\underset{OH}{CH}-\underset{HNC_6H_5}{CH}-COOC_2H_5$ (VI)	 $m\text{-}NO_2C_6H_4-\underset{NH_2}{CH}-\underset{OH}{CH}CO-NH_2$ (VII)
 (III)	 $p\text{-}NO_2C_6H_4-\underset{OH}{CH}-\underset{NHC_6H_5 \cdot HCl}{CH}-COOC_2H_5$ (IV)	 (II)
 (VIII)	 $p\text{-}ClC_6H_4\underset{OH}{CH}-\underset{NHC_6H_5}{CH}-COOC_2H_5$ (IX)	 $p\text{-}ClC_6H_4-\underset{OH}{CH}-\underset{NH_2}{CH}CONH_2$ (X)

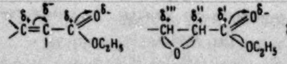
Of the four glycidic esters investigated, only the ethyl esters of β-(m-nitrophenyl)- and β-(p-chlorophenyl) glycidic acids added ammonia. From the reaction of the β-(p-nitrophenyl)- and β-(o-nitrophenyl) glycidic esters with ammonia only the amides of these acids were obtained. It must be noted that this reaction, which was carried out with prolonged heating (to 100°) of a solution of the glycidic esters saturated with ammonia at 0°, proceeded with very severe tarring. The same phenomenon was observed in the investigation of the reaction of ammonia with phenylglycidic esters having electron-donor substituents in the phenyl ring [1]. In connection with the fact that the greater the electron-donor ability of the substituent in the phenyl ring, the smaller was the yield of the ammonia addition product in these cases, we assumed that apparently the amides of the β-hydroxy-α-aminopropionic acids obtained easily split out water in alkaline medium, and the amide of the unsaturated acid resinified.

The delivery of electrons to the β-carbon atom naturally facilitates the splitting out of water and, on the contrary, its impoverishment of electrons as a result of the negative inductive effect of the chlorine in the β-(p-chlorophenyl) glycidic ester should decrease the tendency to splitting out of water from its ammonia addition product. If the formation of the unsaturated acid actually is the cause of resinification, then the reaction of ammonia with the β-(p-chlorophenyl) glycidic ester should proceed with less resinification and give a good yield of the addition product. This, however, was not observed. Attention is attracted by the fact that in all these instances the yield of addition product does not decrease in proportion to the heating of the reaction mixture, as should be expected if it were resinified, but on the contrary it increases. It is obvious that the glycidic esters themselves are unstable upon prolonged heating in alkaline solution. This also is confirmed by the marked resinification when they are saponified with alcoholic alkali.

Proof of the structure of the products of the addition of ammonia to the β-(m-nitrophenyl)- and β-(p-chlorophenyl) glycidic esters was carried out by the previously employed method of oxidation with lead tetraacetate. As a result of the oxidation we obtained in the first case a material with a melting point close to that of m-nitrobenzonitrile. Comparison of its infrared spectrum with the spectrum of m-nitrobenzonitrile and m-nitrobenzaldehyde prepared by known methods showed definitely that the material was m-nitrobenzonitrile with some admixture of m-nitrobenzaldehyde.

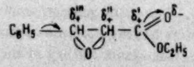
In the case of the oxidation of the product of addition of ammonia to the β-(p-chlorophenyl) glycidic ester, p-chlorobenzaldehyde was obtained. In this same study it was shown that the β-(m-nitrophenyl) glycidic ester adds ammonia predominantly (87%) in the β-position, and the β-(p-chlorophenyl) glycidic ester adds it to the α-carbon atom.

On the basis of our investigations on the opening of the oxide ring upon reaction of β-alkyl- and β-arylglycidic esters with ammonia and aniline, it is possible to attempt to explain the mechanisms discovered by us. At present this reaction is considered from the point of view of its mechanism as a nucleophilic S_N2 substitution [4]. As is known, the rate of such a reaction depends on the steric hindrances around the reaction center, the relative magnitude of its positive charge, and the nucleophilic nature of the molecule attacked. In our case we have two principal possibilities for the direction of attack, namely at the α- or the β-carbon atom. The main course of the reaction in one or the other direction depends on their relative speed, i.e. on the factors just enumerated. The addition of aniline to the β-carbon atom of the β-alkylglycidic esters naturally cannot be effected in the presence of a β-substituent. Therefore it remains to seek a reason in the relative magnitude of the positive charge of the α- and β-carbon atoms. It is known that the oxide ring is capable of transferring its linkage, although considerably less readily than the double bond. Moreover, it is indicated in the literature that the oxide ring can be coupled with a carbonyl group [5]. On this basis we can expect some similarity in the electron shifts in the β-alkylglycidic esters and the ethyl ester of crotonic acid, to which, as is known, nucleophilic agents add in the β-position. Taking into account that in the former the complete loss of any of the electrons of the octet without its disruption is impossible, these electron shifts can be represented by the following diagrams



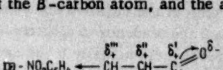
$\delta_+''' > \delta_+'' < \delta_+'$

In a similar manner it is possible to explain the addition of ammonia to all of the phenylglycidic esters studied by us. Owing to the fact that the oxide ring couples less readily than the double bond, the phenyl ring at the demand of the carbonyl group transfers to the β-carbon atom a greater electron density than is further transferred from it to the carbonyl



$\delta_+''' < \delta_+'' < \delta_+'$

As a result of the fact that $\delta_+''' < \delta_+''$, ammonia is added to the relatively more positive α-carbon atom. It is clear that the presence in the para-position of a methyl or methoxy group should strengthen such an effect. In the case of the β-(m-nitrophenyl) glycidic ester the negative induction effect of the m-nitro group leads to impoverishment of the electrons of the β-carbon atom, and the ammonia is added principally in this position



$\delta_+''' > \delta_+'' < \delta_+'$

The circumstance that the β-phenylglycidic ester adds ammonia to the α-carbon atom in spite of the total electron-accepting action of the chlorine, in our opinion supports the determining role of conjugation for the place of opening of the oxide ring. The positive effect of the chlorine linking causes a similar action, as also does the unsubstituted phenyl ring.

The addition of aniline in the α-position of all the β-arylglycidic esters studied by us apparently is explained by a specific mechanism connected with the presence of the phenyl ring in the attacked and attacking molecules. The clarification of this mechanism is not yet possible. Obviously, however, the determining factor here is not an energy factor but a probability factor. The greater stability of the oxide ring in the β-(o-nitrophenyl) glycidic ester, most probably, is caused by the strong effect of the field of the o-nitro group, which makes possible the approach of the nucleophilic agent to the oxide ring.

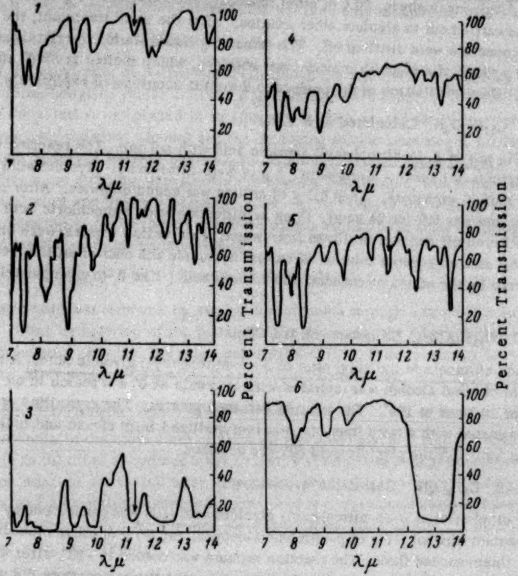


Fig. 2. 1 — $p\text{-}NO_2C_6H_4\text{—}\underset{\diagdown O \diagup}{CH\text{—}CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$, 2 — $m\text{-}NO_2C_6H_4\text{—}\underset{OH}{CH}\text{—}\underset{\substack{NHC_6H_5\\HCl}}{CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$,

3 — $p\text{-}ClC_6H_4\text{—}\underset{\diagdown O \diagup}{CH\text{—}CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$, 4 — $p\text{-}NO_2C_6H_4\text{—}\underset{OH}{CH}\text{—}\underset{\substack{NHC_6H_5\\HCl}}{CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$,

5 — $m\text{-}NO_2C_6H_4\text{—}\underset{\diagdown O \diagup}{CH\text{—}CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$, 6 — $p\text{-}ClC_6H_4\text{—}\underset{OH}{CH}\text{—}\underset{NHC_6H_5}{CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}OC_2H_5$.

We determined the infrared spectra for all the glycidic esters investigated by us and for their reaction products with aniline.* As can be seen from the spectra given (Fig. 2), all the glycidic esters have an absorption frequency in the region 887-906 cm^{-1} that disappears in the corresponding aniline addition products. Only in the case of the β-(o-nitrophenyl) glycidic ester was its disappearance not observed, which confirms our conclusion that reaction of this ester with aniline does not lead to opening of the oxide ring. We already had observed this same absorption frequency in the case of the β-arylglycidic esters with an electron-donor substituent in the phenyl ring [1]. It seems to us, therefore, very probable that this particular frequency is characteristic of the oxide ring.

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* The spectra were measured with an infrared spectrometer made in the Institute of Organo-Chemical Industry of the Ministry of Chemical Industry of the German Democratic Republic in Leipzig. Accuracy of the instrument was ±0.02μ. NaCl prism. Solid materials were measured in potassium bromide tablets.

EXPERIMENTAL

Synthesis of the ethyl ester of β-(o-nitrophenyl) glycidic acid (I) was carried out by the method of Darzens. 75 g of β-o-nitrobenzaldehyde, 70 g of ethyl monochloroacetate, and 34 g of sodium ethylate were used. The reaction was carried out in absolute ether solution. After the usual treatment, the ether and the excess ethyl monochloroacetate were distilled off. The remaining liquid started to crystallize after a short period of standing. 60 g (56%) of a greenish material was obtained, which melted at 62.5° after two recrystallizations from alcohol. Upon distillation of the product (0.2 mm) it decomposed explosively around 170°.

Found %: N 6.1. $C_{11}H_{11}O_5N$. Calculated %: N 5.91.

Reaction of the Na salt of β-(o-nitrophenyl) glycidic acid with aniline. The reaction was carried out according to the instructions of Einhorn – Gernsheim. 1 g of β-(o-nitrophenyl) glycidic acid was dissolved in an aqueous solution of sodium carbonate. Then 0.5 g of aniline was added dropwise. After mixing, the solution became perfectly clear and was left for 24 hours. Upon acidification with hydrochloric acid a precipitate separated, which was filtered off and recrystallized from water. Pale yellow crystals were obtained with m.p. 125-127°. Upon heating with an aqueous solution of barium hydroxide the odor of aniline became evident. The crystals were charred by the action of concentrated sulfuric acid [like β-(o-nitrophenyl)-glycidic acid itself].

Found %: N 9.30. $C_{15}H_{14}O_5N_2$. Calculated %: N 9.28.

An attempt to add ammonia to the ethyl ester of β-(o-nitrophenyl) glycidic acid. A solution of 9 g of the ethyl ester in 30 ml of ethyl alcohol was saturated with ammonia at 0° and sealed in an ampoule. The ampoule was heated for 10 hours to 100°. The solution darkened greatly. The crystalline precipitate that formed, greatly contaminated with a tarry impurity, was recrystallized from dioxan and melted after this at 193-195°. 1.1 g of the amide of the glycidic acid (II) was obtained.

Found %: N 13.72. $C_9H_8O_4N_2$. Calculated %: N 13.46.

Synthesis of the ethyl ester of β-(p-nitrophenyl) glycidic acid (III) was carried out by the method of Darzens. 1 liter of absolute alcohol, 10 g of p-nitrobenzaldehyde, and 80 g of ethyl monochloroacetate were placed in a two-liter, three-necked flask. The reaction mixture was cooled to -12°, after which sodium ethylate (46 g) was added, with continuous stirring, in such a way that the temperature did not rise above -5°. After addition of the sodium ethylate was completed, the mixture was left at room temperature over-night, and then decomposed with water. The ether layer that separated was dried. After the ether was distilled off a dark red liquid remained that quickly crystallized. The crystals were pressed out and recrystallized from 80% ethyl alcohol. 55 g (35%) of barely yellowish crystals were obtained with m.p. 80°.

Found %: C 55.73; H 4.71; N 5.96. $C_{11}H_{11}O_5N$. Calculated %: C 55.69; H 4.64; N 5.90.

Preparation of the hydrochloride of the ethyl ester of β-anilino-α-hydroxy-β-(p-nitrophenyl) propionic acid (IV). 3 g of the ethyl ester of β-(p-nitrophenyl) glycidic acid and 4 g of freshly distilled aniline were dissolved in 40 ml of 96% ethyl alcohol and sealed in an ampoule that was heated for 10 hours at 140-150°. The contents of the ampoule had darkened considerably after this time. The ethyl alcohol and the unreacted aniline were steam-distilled off. The remaining brown mass was dissolved in alcohol and 10 ml of concentrated hydrochloric acid was added to the solution obtained. In several days a white precipitate separated from the mother liquor, the filtrate was drawn off, and the precipitate was washed with anhydrous alcohol. 0.5 g of barely greenish material was obtained with m.p. 173-174° (with decomp.).

Found %: N 7.85. $C_{17}H_{18}O_5N_2 \cdot HCl$. Calculated %: N 7.65.

Addition of ammonia to the ethyl ester of β-(p-nitrophenyl) glycidic acid. A solution of 5 g of the ethyl ester in 30 ml of ethyl alcohol, placed in an ampoule, was saturated with ammonia at 0°. The ampoule was then sealed and heated for 12 hours at 100°. The solution darkened greatly and a dark, crystalline precipitate formed that proved to be the amide of the glycidic acid. It was separated and recrystallized three times from dioxan. M.p. 209-210° (with decomp.).

Found %: N 13.24. $C_9H_8O_4N_2$. Calculated %: N 13.46.

Synthesis of the ethyl ester of β-(m-nitrophenyl) glycidic acid (V) was carried out by the method of Darzens. 100 g of m-nitrobenzaldehyde, 80 g of ethyl monochloroacetate, and 46 g of sodium ethylate were used. After the usual procedure for this method had been carried out, a thick, yellowish liquid was separated, which was then distilled in vacuo. B.p. 180-183° at 1 mm. After some standing it crystallized as white, needle-shaped crystals, which melted after recrystallization from ethyl alcohol at 55.5°. 5 g (35%) was obtained.

Found %: N 5.83. $C_{11}H_{11}O_5N$. Calculated %: N 5.906.

Preparation of the ethyl ester of β-hydroxy-α-anilino-β-(m-nitrophenyl) propionic acid (VI). 5 g of the ethyl ester of β-(m-nitrophenyl)-glycidic acid and 6 g of aniline were dissolved in 30 ml of anhydrous ethyl alcohol, after which the solution was placed in an ampoule that was heated for 18 hours at 130-150°. After completion of the reaction, the ethyl alcohol and the unreacted aniline were steam distilled off and the remaining tarry mass was dissolved in ethyl alcohol. 10 ml of concentrated hydrochloric acid was added to the alcohol solution. After some standing, a mass of white crystals precipitated, which were separated and washed with anhydrous ethyl alcohol and then with absolute ether. 4.5 g (57%) of the white crystals were obtained with m.p. 175-181° (with decomp.). When the crystals were mixed with sulfuric acid, hydrogen chloride was evolved. Upon heating with water the material became liquid.

Found %: N 7.75. $C_{17}H_{18}O_5N_2 \cdot HCl$. Calculated %: N 7.65.

The hydrochloric acid was removed by passing dry ammonia through a suspension in absolute ether of the salt prepared above. After completion of the passage of the ammonia, the ether solution was filtered off from the precipitate of ammonium chloride, the ether was distilled off, and the remaining tarry mass was immersed in a cooling mixture. After prolonged standing it crystallized completely. M.p. 86.0-86.5°.

Found %: N 8.65. $C_{17}H_{18}O_5N_2$. Calculated %: N 8.48.

Addition of ammonia to the ethyl ester of β-(m-nitrophenyl) glycidic acid. A solution of 5 g of the ethyl ester of the acid in 30 ml of anhydrous ethyl alcohol was saturated with ammonia at room temperature. After this the reaction mixture was sealed in an ampoule and heated for 15 hours at 100°. The solution darkened greatly, and upon cooling a crystalline precipitate separated that was considerably contaminated with a tarry impurity. The crystals were purified by repeated recrystallization from dioxan. 1 g of white, needle-shaped crystals was obtained with m.p. 180-181°.

Found %: N 13.49. $C_9H_8O_4N_2$. Calculated %: N 13.46.

A second sample of a solution of 3 g of the ethyl ester of β-(m-nitrophenyl) glycidic acid in 25 ml of ethyl alcohol, saturated at 0° with ammonia, was allowed to stand for 1 month at room temperature in an ampoule. The solution darkened considerably and on the walls of the ampoule pale yellow crystals were formed that were separated from the solution and washed with anhydrous alcohol. 0.5 g (17.5%) was obtained. M.p. 194°.

Found %: N 18.55. $C_9H_{11}O_4N_3$. Calculated %: N 18.66.

Oxidation with lead tetraacetate of the product of the addition of ammonia to the ethyl ester of β-(m-nitrophenyl) glycidic acid (VII). 0.4 g of the addition product described above and 2 g of freshly prepared lead tetraacetate were dissolved in 20 ml of glacial acetic acid. The solution was left for 2 days at room temperature. After this the acid was neutralized with sodium carbonate and the whole mixture was steam-distilled. The white, needle-shaped crystals that had distilled were separated. 0.20 g was obtained. M.p. 102-104°. The substance sublimed readily. Found %: N 17.08. It ensued from the infrared spectral investigation of the material that it was a mixture of m-nitrobenzonitrile (87%) and m-nitrobenzaldehyde (13%).

Synthesis of the ethyl ester of β-(p-chlorophenyl) glycidic acid (VIII). p-Chlorobenzaldehyde was prepared by the chlorination of p-chlorotoluene. The synthesis was carried out by Darzens' method. 100 g of p-chlorobenzaldehyde, 88 g of ethyl monochloroacetate, and 46 g of sodium ethylate were used for the reaction. The reaction was carried out in absolute ether solution (700 ml). After the usual treatment of the reaction mixture for this method 70 g (45%) of a liquid was obtained that was then distilled in vacuo.

B.p. 160° at 1 mm, d^{20}_4 1.2527, n^{20}D 1.5458. MR$_D$ 57.06; Calculated. 55.36; EMR$_D$ 1.70.

Found %: C 58.30; H 4.73. $C_{11}H_{11}O_3Cl$. Calculated %: C 58.27; H 4.85.

Preparation of the ethyl ester of β-hydroxy-α-anilino-β-(p-chlorophenyl) propionic acid (IX). 5 g of the ethyl ester of β-(p-chlorophenyl) glycidic acid and 6 g of aniline were sealed in an ampoule, which was heated for 8 hours at 140-145°. The reaction mass was vacuum distilled. At 190° (1 mm) a pale yellow, thick liquid distilled, which crystallized upon long standing. 4 g (57%) was obtained.

Found %: N 4.25. $C_{17}H_{18}O_3NCl$. Calculated %: N 4.38.

Preparation of the amide of β-hydroxy-α-amino-β-(p-chlorophenyl) propionic acid (X). A solution of 10 g of the ethyl ester of β-(p-chlorophenyl) glycidic acid in 30 ml of ethyl alcohol was saturated with ammonia at 0° and sealed in an ampoule, which was held for 36 hours at room temperature and then heated at 100°. Upon cooling, a white crystalline precipitate separated out, which melted at 182° after recrystallization from aqueous alcohol. 1.7 g (18%) was obtained.

Found %: C 50.34; H 5.03; N 13.02. $C_9H_{11}O_2N_2Cl$. Calculated %: C 50.34; H 5.03; N 13.10.

Oxidation of the amide of β-hydroxy-α-amino-β-(p-chlorophenyl) propionic acid with lead tetraacetate. To a solution of 1.0 g of the amide in 25 ml of glacial acetic acid was added 3.5 g of freshly prepared lead tetraacetate. The reaction mixture was left at room temperature for two days. After this the acetic acid was neutralized with sodium hydroxide, whereupon a white crystalline precipitate separated out, which was pressed out and melted without additional purification at 40-42°. 0.46 g (70%) was obtained. From the crystalline precipitate a quantitative yield of phenylhydrazone was obtained with m.p. 125-126° (in the literature the m.p. 127° is given for the phenylhydrazone of p-chlorobenzaldehyde).

Found %: N 12.28. $C_{13}H_{11}N_2Cl$. Calculated %: N 12.15.

SUMMARY

1. The reactions of aniline and ammonia with the ethyl esters of β-(o-nitrophenyl)-, β-(m-nitrophenyl)-, β-(p-nitrophenyl)-, and β-(p-chlorophenyl) glycidic acids have been investigated.

2. It has been established that the ethyl esters of β-(m-nitrophenyl)-, β-(p-nitrophenyl)-, and β-(p--chlorophenyl) glycidic acids add aniline in the α-position. Ammonia is added to the β-(p-chlorophenyl) glycidic ester in the α-position, but to the β-(m-nitrophenyl) ester predominantly in the β-position. The β-(p-nitrophenyl) glycidic ester does not add ammonia at all.

3. It has been shown that the ethyl ester of β-(o-nitrophenyl) glycidic acid does not add either aniline or ammonia.

4. The reaction of the Na salt of β-(o-nitrophenyl) glycidic acid with aniline has been studied. It has been shown that in this case a product of addition to the oxide ring of the glycidic acid salt is not obtained. The data in the literature to the effect that the addition reaction takes place are erroneous.

5. The infrared spectra of all the aromatic glycidic esters investigated by us and of their aniline addition products have been determined. Absorption maxima have been marked that most probably are characteristic of the oxide ring.

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Received February 16, 1957

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*Original Russian pagination. See C. B. Translation.

INVESTIGATION OF COMPOUNDS CONTAINING A THREE-MEMBERED OXIDE RING

XXI. REACTION OF AMIDES OF β-TETRA- AND β-PENTAMETHYLENEGLYCIDIC ACIDS WITH HEXYL- AND BENZYLAMINES

V. F. Martynov and Zh. D. Vasiutina

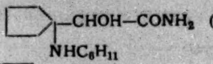
In one of the previous communications [1] an investigation of the reaction of aliphatic and aliphatic-aromatic amines with the amide of β,β'-dimethylglycidic acid has been described. The present work is a continuation of this investigation.

The reaction of the amides of β-tetra- and pentamethyleneglycidic acids and hexyl- and benzylamines was accomplished by heating their alcohol solutions in sealed ampoules at 100 or 120-130°. The more reactive proved to be the amide of β-tetramethyleneglycidic acid, which gave comparatively good yields of addition products with both amines. For purposes of comparison we carried out the reaction of cyclohexylamine with the potassium salt of β-tetramethyleneglycidic acid, but in this case a lower yield of the addition product was obtained. The amide of β-pentamethyleneglycidic acid appeared less reactive. With hexylamine, reaction did not take place at all, in spite of the fact that we carried out the reaction at 150°. It is obvious that such a result is explained by steric hindrances, by virtue of which the two cyclohexane rings, which as is known have a nonplanar structure, cannot rest in direct proximity to one another. This, by the way, again confirms that opening of the oxide ring of β-dialkyl-substituted glycidic acids occurs at the β-carbon atom, because otherwise the reaction might go in the direction of addition to the α-carbon atom, which however has never been observed. With benzylamine the reaction takes place, it is true, under somewhat more severe conditions (heating to 120-130°). In this case, as is understandable, the steric hindrances are considerably less active.

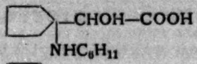
We attempted to prepare benzoyl derivatives for the addition products — the amides of the hydroxyamino acids that we obtained — but this attempt succeeded only with the addition product of cyclohexylamine to the potassium salt of β-tetramethyleneglycidic acid. By the Schotten-Baumann method [2] the corresponding N-benzoyl derivative was obtained.

For evidence of the structure of the addition products we took advantage of the action of concentrated sulfuric acid [1]. Upon heating the amide of hydroxycyclohexylamino-β-tetramethylenepropionic acid with sulfuric acid at 150-160°, copious evolution of gas bubbles (carbon monoxide) began, which to a certain extent already might indicate the structure of the addition compound. After the usual treatment of the reaction mixture, in these instances we succeeded in isolating α-cyclohexylamino-α-tetramethyleneacetaldehyde as its 2,4-dinitrophenylhydrazone. It was possible to conclude that the oxide ring in the indicated glycidic acid amide was opened at the β-carbon atom. Regrettably, this method of proof, which gives good yields of decomposition products for the addition products of aromatic amines, gives very low yields in the case of aliphatic amines. This is explained, in all probability, by the fact that the aminoaldehydes obtained in this way which contain aliphatic radicals undergo further conversion to resinous products, while the aminoaldehydes that contain aromatic radicals are stabilized as a result of conversion to indoles. We tried to decrease the temperature limits of the breakdown by using not the amides of the hydroxyamino acids, but the free acids; in this case breakdown set in at a lower temperature (100-120°); however, even under such experimental conditions an increase in yields of the aminoaldehydes was not observed.

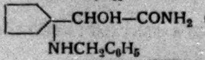
The product obtained by reaction of the amide of β-tetramethyleneglycidic acid with benzylamine also was subjected, in the form of the free acid, to reaction with sulfuric acid. Decomposition with copious evolution of carbon monoxide took place at 100-110°. This indicated the presence of an α-hydroxy-β-amino acid; however, the nature of the second fragment of the molecule was not clarified by us. We ascribed a structure to the compound that was obtained by the reaction of the amide of β-pentamethyleneglycidic acid with benzylamine by analogy with the previously studied compounds. The structural formulas for the compounds obtained are presented below.



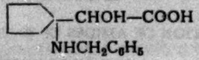
(I)



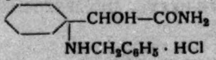
(II)



(III)



(IV)



(V)

EXPERIMENTAL

Preparation of the amide of α-hydroxy-β-cyclohexylamino-β-tetramethylenepropionic acid (I). 5 g of the amide of β-tetramethyleneglycidic acid dissolved in 30 ml of anhydrous ethyl alcohol and 4.5 g of cyclohexylamine was sealed in an ampoule, which was heated for 6 hours at 100°. After the heating of the reaction mixture was completed, part of the ethyl alcohol (10-15 ml) was distilled off in vacuo. From the remaining liquid, crystals precipitated in several hours that melted at 127-128° after recrystallization from 96% alcohol. Yield 4.3 g (50.6%).

Found %: N 11.56. $C_{13}H_{24}O_2N_2$. Calculated %: N 11.67.

Decomposition of the amide (I) by the action of concentrated sulfuric acid. To 5 g of the compound was added 35 ml of concentrated sulfuric acid. The mixture was heated on a bare flame while being stirred. At 150-160° copious evolution of gas bubbles (carbon monoxide) began and the solution darkened. When the evolution of bubbles slowed down, the hot liquid was poured onto ice. When the reaction mixture was neutralized with sodium hydroxide solution, there separated out an emulsion of cyclohexylaminotetramethyleneacetaldehyde, which was steam-distilled off. The aminoaldehyde was extracted with ether from the distillate. After being dried with potash, the ether was distilled off and the residue was distilled in vacuo. At 140-144° (5 mm) a small amount of a viscous, yellowish liquid passed over, which was combined with 2,4-dinitrophenylhydrazine. As a result, crystals of the 2,4-dinitrophenylhydrazone of cyclohexylaminotetramethyleneacetaldehyde precipitated, which melted at 123-125° after recrystallization from ethyl alcohol.

Found %: N 18.96. $C_{18}H_{25}O_4N_5$. Calculated %: N 18.67.

Preparation of α-hydroxy-β-cyclohexylamino-β-tetramethylenepropionic acid (II). 3 g of the amide of α-hydroxy-β-cyclohexylamino-β-tetramethylpropionic acid was refluxed with 50 ml of 50% sulfuric acid for 8 hours. The sulfuric acid was precipitated with barium carbonate until there was a negative reaction for SO_4'' ion. The filtrate was evaporated on a water bath. As a result, white crystals of the hydroxyamino acid were obtained, which melted at 206-207° (with decomp.) after recrystallization from water. 1.75 g (58%) was obtained.

Found %: N 5.95. $C_{13}H_{23}O_3N$. Calculated %: N 5.81.

Preparation of the potassium salt of β-tetramethyleneglycidic acid. To a solution of 3.5 g of potassium hydroxide in anhydrous ethyl alcohol was added 10 g of the ethyl ester of β-tetramethyleneglycidic acid. Almost at once a white precipitate of the potassium salt of β-tetramethyleneglycidic acid separated. The yield was quantitative.

Reaction of the potassium salt of β-tetramethyleneglycidic acid with cyclohexylamine. 5 g of the potassium salt of β-tetramethyleneglycidic acid and 3.5 g of cyclohexylamine were dissolved in anhydrous ethyl alcohol. The solution obtained was sealed in an ampoule that was heated at 100° for 6 hours. As a result of the reaction, a dark, viscous liquid was obtained that started to crystallize in a few days. 2.6 g (34%) of the potassium salt of α-hydroxy-β-cyclohexylamino-β-tetramethylenepropionic acid was obtained.

Preparation of the benzoyl derivative of α-hydroxy-β-cyclohexylamino-β-tetramethylenepropionic acid was carried out by the Schotten-Baumann method [2]. 0.5 g of the potassium salt of α-hydroxy-β-cyclohexylamino-β-tetramethylenepropionic acid was dissolved in a small amount of 10% aqueous NaOH solution. To this solution was added gradually an excess (0.4 g) of benzoyl chloride. The mixture was shaken vigorously. The unreacted benzoyl chloride was decomposed by heating on the water bath. The precipitate of benzoyl derivative that had been formed was filtered off, washed with water until the alkali was completely removed, and dissolved in aqueous ethyl alcohol. To the solution obtained there was added dilute hydrochloric acid (1 : 1), after which a white precipitate separated out, which was filtered off and recrystallized from 40-45% aqueous ethyl alcohol. 0.21 g of the benzoyl derivative was obtained, which amounted to 34%.

Found %: N 4.5. $C_{20}H_{27}O_4N$. Calculated %: N 4.06.

Preparation of the amide of α-hydroxy-β-benzylamino-β-tetramethylenepropionic acid (III). 5 g of the amide of β-tetramethyleneglycidic acid and 4.7 g of benzylamine were dissolved in 20 ml of anhydrous ethyl alcohol and sealed in an ampoule that was heated for 8 hours at 100°. The next day crystals of the amide precipitated. Yield 4.2 g (48%). After recrystallization from 96% ethyl alcohol the compound melted at 53-54°.

Found %: N 11.45. $C_{14}H_{20}O_2N_2$. Calculated %: N 11.29.

Preparation of α-hydroxy-β-benzylamino-β-tetramethylenepropionic acid (IV). 2 g of the amide (III) was refluxed with 50 ml of 50% sulfuric acid for 8 hours. The sulfuric acid was neutralized by boiling the solution with barium carbonate until there was a negative reaction for SO_4'' ion. The filtrate was evaporated on a water bath. 1.1 g (55%) of the acid was obtained. After recrystallization from ethyl alcohol the melting point in a sealed capillary was 228-229° (with decomp.).

Found %: N 5.75. $C_{14}H_{19}O_3N$. Calculated %: N 5.62.

Preparation of the amide of α-hydroxy-β-benzylamino-β-pentamethylenepropionic acid (V). A mixture of 5 g of the amide of pentamethylenepropionic acid dissolved in 30 ml of ethyl alcohol with 4 g of benzylamine was sealed in an ampoule and heated for 8 hours at 120-130°. A dark, viscous liquid was obtained that did not crystallize upon prolonged standing. From this reaction mass the unreacted benzylamine was steam distilled off, after which concentrated hydrochloric acid was added to the residue. A white precipitate of the hydrochloride of the amide separated out. 3.2 g (33%) was obtained. After recrystallization from aqueous alcohol the m.p. was 222-223° (with decomp.).

Found %: N 9.43. $C_{15}H_{23}O_2N_2Cl$. Calculated %: N 9.38.

SUMMARY

1. The reaction of the amides of β-tetra- and β-pentamethyleneglycidic acids with cyclohexyl- and benzylamines has been studied. It has been found that the amide of β-tetramethyleneglycidic acid is more reactive than the amide of β-pentamethyleneglycidic acid.

2. It has been shown that opening of the oxide ring of the amides of the indicated glycidic acids occurs at the α-carbon atom. All the addition products were prepared for the first time.

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Received February 16, 1957

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* Original Russian pagination. See C. B. Translation.

REACTIONS OF HALOMETAL ALCOHOLATES

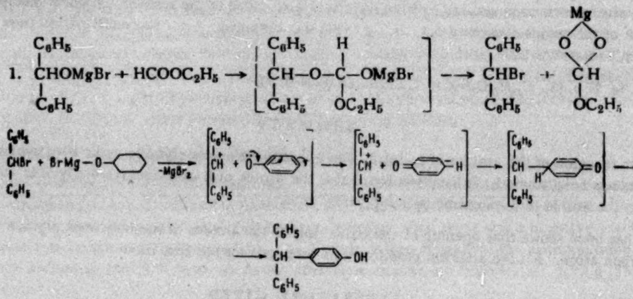
VI. A NEW METHOD OF SYNTHESIS OF MONOHYDROXYTRIARYLMETHANES

I. I. Lapkin and M. I. Belonovich

As a result of previous investigations [1] it has been established that the action on halomagnesium diarylcarbinolates of esters of formic or oxalic acid used in equimolecular amounts with respect to the carbinolate leads to the formation of diarylmethyl halides. It also has been established that halomagnesium phenolates and naphtholates under the same conditions do not react with the esters mentioned. This circumstance was used by us to work out a method for the preparation of monohydroxytriarylmethanes.

The essence of this method is that a mixture of the diarylcarbinol and phenol or naphthol is converted by the addition of the appropriate amount of ethylmagnesium bromide to a mixture of bromomagnesium diarylcarbinolate and phenolate. Subsequent addition to the reaction mixture of an ester of oxalic acid converts the bromomagnesium diarylcarbinolate to diarylmethyl bromide, which, reacting with the bromomagnesium phenolate (or naphtholate) that is unchanged under these conditions, forms a monohydroxytriarylmethane.

As an intermediate product in this reaction we might suggest the formation of an aryl diarylmethyl ether, which rearranges then to the hydroxytriarylmethane, but since this ether has not been detected in the reaction products, the mechanism of the reaction under investigation may be represented by the following more probable scheme



That the ethers are not intermediate products of this reaction is also indicated by the fact that the products of carbinol or phenol rearrangements discovered by Schorigin [2] and characteristic of the specific group of ethers were not observed in the reaction studied.

A great deal of work has been devoted to the investigation of the condensation of aromatic alcohols with phenols. Some facts also have been recorded concerning the condensation of benzhydrol (and benzhydryl halides) with phenols. It has been established [3] that upon heating phenol and diphenylmethyl bromide on a water bath p-hydroxytriphenylmethane is formed, while heating sodium phenolate with this bromide leads to the formation of o-hydroxytriphenylmethane. The experiments of Schorigin [4] have shown that by the action of diphenylmethyl bromide on sodium phenolate there is produced, in addition to the phenyl ether of benzhydrol, a small amount of o-hydroxytriphenylmethane. The reaction of benzhydrol and phenol in benzene solution and in the presence of $SnCl_4$ [5] leads to the formation of p-hydroxytriphenylmethane. Experiments [6] investigating the reaction of diphenylmethyl chloride with phenol in the presence of $ZnCl_2$ at 110° also led to these results. p-Hydroxytriphenylmethane also is obtained from benzhydrol and phenol in carbon bisulfide in the presence of $AlCl_3$ [7]. A similar condensation takes place with p-cresol. Upon heating benzhydryl bromide with p-cresol at 150° or with sodium p-cresolate at 50-60°, and also upon boiling with sodium p-cresolate in ether, 3-methyl-6-hydroxytriphenylmethane is obtained [3]. The reaction of benzhydrol with o-cresol in a mixture of glacial acetic acid and sulfuric acid on a boiling water bath results in the formation of 3-methyl-2-hydroxytriphenylmethane [8].

In contrast to the results of investigations [3] and [4], according to which o-hydroxytriphenylmethane is formed by the reaction of diphenylmethyl bromide with sodium phenolate, in the reaction under investigation of bromomagnesium phenolate and also of bromomagnesium o-cresolate with diphenylmethyl bromide, which is obtained as indicated above in the reaction of bromomagnesium benzhydrolate and the esters of oxalic acid, the p-isomers of hydroxytriarylmethanes are produced, and to be precise, p-hydroxytriphenylmethane. The ortho-isomers are produced only if the para-position is occupied. For example, when p-cresol is used in the reaction under study, 5-methyl-2-hydroxytriphenylmethane is formed, i.e. the benzhydryl radical is in the ortho-position relative to the hydroxyl group. This same radical when it enters into the α-naphthol molecule, occupies the 4-position, and in the β-naphthol molecule the α-position.

EXPERIMENTAL

1. Synthesis of 4-hydroxytriphenylmethane. Benzhydrol and phenol (1/15 mole each) were dissolved in three times their volume of anhydrous diethyl ether and to this solution was added an ether solution (3 volumes) of ethylmagnesium bromide (2/15 mole). To the resulting ether solution of bromomagnesium benzhydrolate and phenolate was added diethyl oxalate (1/15 mole), after which the reaction mixture was heated for 3 hours, then decomposed with water and 10% acetic acid, the ether layer was separated from the water and washed with a 10% sodium bicarbonate solution and water. After the ether solution was dried with calcined sodium sulfate, the solvent was distilled off and the reaction product was distilled in vacuo. The main fraction (13 g), which distilled at 190-200° (7 mm), crystallized in the receiver and was purified by recrystallization from petroleum ether. M.p. 110°. Yield 76%.

Found %: C 87.57; H 6.16; OH 6.1. $C_{19}H_{16}O$. Calculated %: C 87.66; H 6.20; OH 6.5.

In the literature m.p. 109° [5] and 112° [3] are indicated for 4-hydroxytriphenylmethane.

2. 3-Methyl-4-hydroxytriphenylmethane was prepared under the conditions indicated above and with the same amounts of the starting materials; instead of phenol, o-cresol was used. The reaction product was distilled in vacuo (6 mm) at 195-205°. By recrystallization from a mixture of petroleum ether and toluene (3 : 1) colorless crystals were obtained with m.p. 102°. Yield 12 g (66%). In the literature the m.p. 100° is indicated [9] for 3-methyl-4-hydroxytriphenylmethane prepared from 3-methyl-4-hydroxytriphenylcarbinol by boiling with zinc and glacial acetic acid.

Found %: C 87.38; H 6.49; OH 6.00. $C_{20}H_{18}O$. Calculated %: C 87.55; H 6.62; OH 6.20.

3. Synthesis of 5-methyl-2-hydroxytriphenylmethane. The reaction conditions were as indicated above. The starting materials – benzhydrol and p-cresol – were used in amounts of 1/15 mole. After vacuum distillation the reaction product was purified by recrystallization from a mixture of petroleum ether and toluene (3 : 1) and showed a m.p. of 135°. Yield 12.5 g (70%). According to [3], m.p. 135°.

Found %: C 87.35; H 6.45; OH 6.1. $C_{20}H_{18}O$. Calculated %: C 87.55; H 6.62; OH 6.2.

4. Synthesis of diphenyl-(4-hydroxynaphthyl-1)methane. The starting materials – benzhydrol, α-naphthol, and diethyl oxalate – were used in amounts of 2/15 mole. Since diphenyl-(4-hydroxynaphthyl-1) methane decomposes on vacuum distillation, the crystalline reaction product was purified by recrystallization from a mixture of petroleum ether and toluene. M.p. 171-172°. Yield 70%. According to [10], m.p. 170--171.5°.

Found %: C 88.78; H 5.76; OH 5.40. $C_{23}H_{18}O$. Calculated %: C 89.00; H 5.85; OH 5.50.

5. Synthesis of diphenyl-(2-hydroxynaphthyl-1)methane was carried out under the conditions indicated in the preceding experiments, from bromomagnesium benzhydrolate, β-naphtholate, and diethyl oxalate (1/15 mole each). After the ether was distilled off, the compound crystallized and was purified by recrystallization. M.p. 110° (from a mixture of petroleum ether and toluene). Yield 18 g (70%).

Found %: C 88.81; H 5.71; OH 5.20. $C_{23}H_{18}O$. Calculated %: C 89.00; H 5.85; OH 5.50.

For proof of the structure of the compound obtained, diphenyl-(2-ethoxynaphthyl-1) carbinol was first synthesized from benzophenone and 2-ethoxynaphthylmagnesium bromide (1/15 mole each) under the usual conditions for organomagnesium reactions. M.p. 156° (from a mixture of petroleum ether and toluene). Yield 40 g (56%).

Found %: C 84.52; H 6.18; OH 4.70; OC_2H_5 11.8. $C_{25}H_{22}O_2$. Calculated %: C 84.71; H 6.26; OH 4.80; OC_2H_5 12.7.

By heating the diphenyl-(2-ethoxynaphthyl-1) carbinol, dissolved in 98% acetic acid, with zinc dust for 3 hours diphenyl-(2-hydroxynaphthyl-1)-methane was obtained. M.p. 110°.

Found %: C 88.79; H 5.72; OH 5.3. $C_{23}H_{18}O$. Calculated %: C 89.00; H 5.85; OH 5.5.

A mixed melting point test with the compound obtained by the reaction under investigation showed no depression.

SUMMARY

1. A new method has been developed for the synthesis of monohydroxytriarylmethanes which is based on the action of oxalic acid esters on an equimolecular mixture of bromomagnesium diarylcarbinolates and phenolates (or naphtholates), and mechanisms have been shown for this reaction.

2. In this investigation two compounds not previously described were synthesized – diphenyl-(2-hydroxynaphthyl-1) methane and diphenyl-(2-ethoxynaphthyl-1) carbinol.

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Received March 7, 1957

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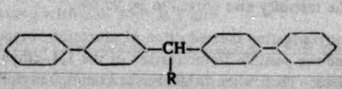
* Original Russian pagination. See C. B. Translation.

METALLOORGANIC SYNTHESIS OF DIBIPHENYLALKANES AND DIPHENYLALKANES. III

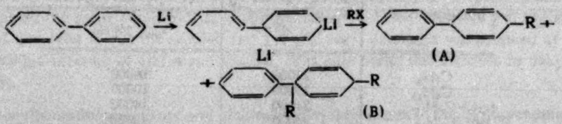
A. D. Petrov, E. P. Kaplan, Z. I. Letina and Iu. P. Egorov

In preceding communications [1,2] the synthesis of hydrocarbons of the dibiphenylalkane and alkyl-1,4-dihydrodiphenyl series has been described. In the present communication the results are reported of additional investigations on the synthesis of these series of hydrocarbons. By the reaction of 4-diphenylmagnesium bromide with the ethyl ester of undecylenic and palmitic acids, alcohols were obtained which were dehydrated to olefins and then hydrogenated stepwise over Raney nickel to naphthenic hydrocarbons. The freezing points and the viscosities at different temperatures were determined for the hydrocarbons obtained. It was established that with lengthening of the alkyl radical up to a certain limit, in spite of the increase of molecular weight, the freezing point falls, but then rises sharply



	freezing point
CH_3	+46°
C_3H_7	+20
C_7H_{15}	+2
$C_{10}H_{21}$	−3
$C_{15}H_{31}$	+55

The viscosity of the hydrocarbons decreases with an increase in the alkyl chain, but the index of viscosity is almost unchanged (Fig. 1). According to the work of Schlenk and Bergmann [3] lithium is added to diphenyl in the 1,4-position, forming 1,4-dilithiumdihydrodiphenyl. By the action on the latter of n-C_4H_9Br and n-$C_{10}H_{19}$Br, we obtained monoalkyldihydrodiphenyls and dialkyldihydrodiphenyls.



All the 4-monoalkyl-1,4-dihydrodiphenyls solidify in crystalline form, but 1,4-dialkyl-1,4-dihydrodiphenyls, in spite of the large molecular weight, have freezing points considerably lower and solidify in the form of a glass.

R	m.p. (A)	F.p. (B)
C_4H_9	−1°	−19° (glass)
C_6H_{13}	+7	−25 (glass)
$C_{10}H_{21}$	+36	−17 (glass)

To establish the position (1 or 4) of the alkyl chain in the monoalkyldihydrodiphenyls, the dehydrogenation of n-C_4H_9- and n-C_6H_{13}-1,4-dihydrodiphenyls was carried out with sulfur. The 4-butyl- and 4-hexyldiphenyls agreed well as to freezing point with the freezing points of these hydrocarbons prepared previously by another method [4]. This indicates that the alkyl chains in the monoalkyldihydrodiphenyls are in the 4-position.

Ultraviolet absorption spectra* were determined for the compounds synthesized. The spectra of the mono- and disubstituted compounds were similar to each other and differed only in the intensity of the principal band (see Table). The spectra obtained raise doubts as to the correctness of the structure ascribed to the compounds synthesized. If we compare the spectra of our compounds (Fig. 2) with the spectra of diphenyl and 1-phenylcyclohexene, their similarity can be definitely seen, particularly in the magnitude of the intensity at the maximum.

From the literature it is known that the intensity of the band ~250 – 260 mμ in aromatic compounds does not exceed 300 units for a single ring, but it increases considerably when this ring is conjugated with the C = C, C =O, and other bonds. For example, the intensity of the maximum of the band in toluene is ~250, in triphenylmethane 900, and in styrene 12,000 units. In diphenyl, where there are conjugated C = C bonds, the intensity of the band is 20,000. In our compounds, to which we had up to now, following Schlenk and Bergmann [3], ascribed an unconjugated structure (quinoid structure of the II ring), the intensity also proved to be 20,000.

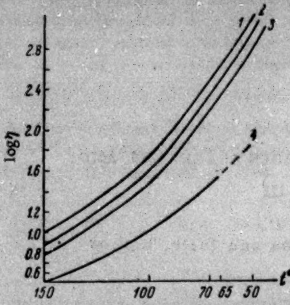
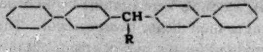


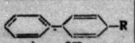
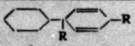
Fig. 1. Viscosity curves of hydrocarbons:



$1 - R = C_3H_7$, $2 - R = C_7H_{15}$, $3 - R = C_{10}H_{21}$, $4 - R = C_{18}H_{37}$.

Recently Benkeser and co-workers [5], investigating the reduction of aromatic compounds with lithium in the medium of aliphatic amines, suggested the possible isomerization of the 1,4-dihydroaromatic compounds obtained to the more stable conjugated systems. Thus, when lithium acted on diphenyl, 1-cyclohexylcyclohexene was formed. When anisole was reduced [6], a mixture was obtained consisting of 53% 2,5-dihydroanisole and 47% 2,3-dihydroanisole.

Intensity of Maximum of Principal Absorption Band

Meaning of R	 λ_{max} 253 mμ	 λ_{max} 248 mμ
C_4H_9	24000	16200
C_6H_{13}	17000	10000
tert.-C_8H_{17}	21000	14000
iso-.C_8H_{17}	24000	13000
C_9H_{19}	17000	12000
$C_{10}H_{21}$	20000	6000

Examining the data obtained by us from the UV spectra, we can propose that in our case also partial isomerization took place with the formation of a mixture of 4-alkyl-1,4-dihydrodiphenyl and 4-alkyl-2,3-dihydrodiphenyl. With such an assumption, obviously, we should expect spectra similar to the diphenyls both in position and in intensity. For the disubstituted compounds there also is possible the formation of a mixture of 1,4-dialkyl-1,4-dihydrodiphenyl with other isomers of the dialkyldihydrodiphenyls (for example, with 3,4-dialkyl-3,4-dihydrodiphenyl), which probably explains also the sharp lowering of the freezing point of the dialkyldihydrodiphenyls. The intensity of the principal band also is changed depending on the percentage composition of the isomers.

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*UV spectra were determined by I. N. Lifanova, for which the authors express their deep appreciation. The spectra were taken in an ISP-22 spectrograph in isooctane solution. A hydrogen lamp of the Ostroumov type was used as a uniform source of emission.

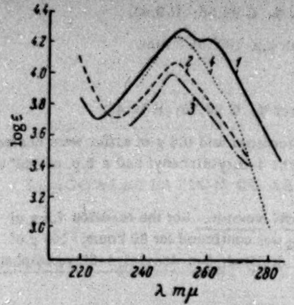
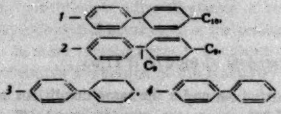


Fig. 2. Ultraviolet absorption spectra.



EXPERIMENTAL

1. Synthesis of dibicyclohexyldecylmethane. a) Preparation of dibiphenylundecadiene. To 20 g of Mg in 100 ml of ether was added over a period of 12 hours at 30-33° 257 g of 4-bromodiphenyl dissolved in 700 ml of ether. Then 106 g of ethyl undecylenate was added, after which the reaction mixture was stirred for 12 hours more at 40-45°. It was decomposed with 10% CH_3COOH. The ethereal portion of the solution was separated and the insoluble tetraphenyl was filtered off. 50 g of a product with b.p. 300-330° at 3 mm was isolated which represented, according to its analysis, a mixture of olefin and alcohol. To obtain the pure olefin the mixture was dehydrated with CH_3COOH and H_2SO_4 [7]. The olefin, distilled over sodium, had a b.p. of 295-298° at 3 mm.

Found %: C 92.18, 92.20; H 7.16, 7.14. $C_{35}H_{36}$. Calculated %: C 92.10; H 7.89.

b) Hydrogenation of the double bond in the chain. In an autoclave with a volume of 0.5 l were placed 15 g of olefin, 100 ml of dimethylcyclohexane, and 3 g of Raney nickel. The initial pressure was 60 atm., hydrogenation temperature 200°. A vaseline-like product was obtained with b.p. 300° at 3 mm.

Found %: C 91.72, 91.85; H 8.31, 8.22. $C_{35}H_{40}$. Calculated %: C 91.30; H 8.69.

c) Hydrogenation of aromatic rings. In an autoclave were placed 13 g of hydrocarbon, 140 ml of dimethylcyclohexane, and 6 g of Raney nickel. Initial pressure 100 atm, hydrogenation temperature 230-250°. The dibicyclohexyldecylmethane had a b.p. of 270-272° at 3 mm.

F.p. −3°, n^{20}_D 1.5080, ν_{50} 5.7595 st.*, ν_{100} 0.2840 st., ν_{150} 0.0610 st.

Found %: C 87.02, 87.12; H 13.01, 13.01. $C_{35}H_{64}$. Calculated %: C 86.77; H 13.22.

2. Synthesis of dibicyclohexylpentadecylmethane. a) Preparation of dibiphenylpentadecenemethane was carried out under the same conditions as in the preceding synthesis. From 24 g of Mg and 344 g of 4-bromodiphenyl dissolved in 700 ml of ether and 142 g of ethyl palmitate was obtained 40 g of a crystalline product representing a mixture of olefin and alcohol. The pure olefin was obtained by dehydration with acetic and sulfuric acids.

b) Dibiphenylpentadecylmethane was obtained by hydrogenation of the corresponding olefin. 13 g of hydrocarbon, 100 ml of dimethylcyclohexane, and 3 g of Raney Ni were used in the charge. Initial pressure 100 atm, hydrogenation temperature 200°. A hydrocarbon was obtained with m.p. 120°.

Found %: C 90.12, 90.23; H 10.00, 9.87. $C_{40}H_{50}$. Calculated %: C 90.56; H 9.43.

c) Hydrogenation of aromatic rings. 10 g of hydrocarbon, 100 ml of dimethylcyclohexane, and 6 g of Raney Ni were used in the charge. Initial pressure 110 atm, hydrogenation temperature 235-250°. The dibicyclohexylpentadecylmethane obtained had a m.p. of 55°.

ν_{100} 0.1018 st., ν_{150} 0.0340 st.

Found %: C 86.77, 86.80; H 13.10, 13.11. $C_{40}H_{74}$. Calculated %: C 86.66; H 13.33.

3. Reaction of 1,4-dilithium-1,4-dihydrodiphenyl with n-butyl bromide. A description of the experiment has been given in a preceding communication [2]. In the reaction 77 g of diphenyl, 7 g of lithium, and 400 ml of ether were used. The mixture was shaken for 80 hours. 137 g of n-butyl bromide was added. A total of 35 g of alkylbiphenyls was obtained. After repeated distillation 20 g of 4-butyl-1,4-dihydrodiphenyl was isolated, b.p. 152° at 3 mm.

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*st. = stoke — publisher's note.

Found %: C 90.59, 90.44; H 9.52, 9.33. $C_{16}H_{20}$. Calculated %: C 90.56; H 9.43.

15 g of 1,4-dibutyl-1,4-dihydrodiphenyl also was isolated with b.p. 189° at 3 mm.

$n^{20}D$ 1.5272, d^{20}_4 0.9285, MR_D 88.76; calculated 88.91.

Found %: C 89.18, 89.11; H 10.82, 10.90. $C_{20}H_{28}$. Calculated %: C 89.55; H 10.45.

Dehydrogenation of 4-butyl-1,4-dihydrodiphenyl. 5 g of hydrocarbon and 0.6 g of sulfur were heated for 4 hours at 200-220°. The hydrocarbon was distilled over sodium. The 4-butyldiphenyl had a b.p. of 140° at 3 mm, f.p. +15°. Literature data [4]: f.p. +16°, $n^{20}D$ 1.5739.

4. Reaction of 1,4-dilithium-1,4-dihydrodiphenyl with n-decyl bromide. For the reaction 7.5 g of lithium, 77 g of diphenyl, and 600 ml of ether were taken. Shaking was continued for 80 hours. 105 g of n-decyl bromide was added. 29 g of alkylbiphenyls were obtained. Isolated: 4-n-decyl-1,4-dihydrodiphenyl, 19 g, b.p. 220-222° at 3 mm.

Found %: C 89.71, 89.51; H 10.55, 10.49. $C_{22}H_{32}$. Calculated %: C 89.18; H 10.81.

1,4-Di-n-decyl-1,4-dihydrodiphenyl, 10 g.

$n^{20}D$ 1.5040; d^{20}_4 0.8964, MR_D 143.68; calculated 143.0.

Found %: C 87.59, 87.62; H 12.44, 12.40. $C_{32}H_{52}$. Calculated %: C 88.07; H 11.93.

5. Dehydrogenation of 4-hexyl-1,4-dihydrodiphenyl was carried out under the same conditions as for 4-butyl-1,4-dihydrodiphenyl. The 4-hexyldiphenyl had a m.p. of 25°. Literature data [4]: m.p. +28°.

SUMMARY

1. Dibicyclohexyldecylmethane and dibicyclohexylpentadecylmethane have been synthesized. Their viscosity characteristics have been determined.

2. 4-Butyl-, 1,4-dibutyl-, 4-decyl-, and 1,4-didecyl-1,4-dihydrodiphenyl have been prepared.

3. The UV spectra of 12 alkyl-1,4-dihydrodiphenyls have been determined and it has been shown that in the organolithium synthesis of the indicated forms conjugated structures are produced for the most part, along with compounds having a quinoid structure.

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Received January 16, 1957

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*Original Russian pagination. See C. B. Translation.

SILICOALKYLATION OF AROMATIC COMPOUNDS BY DICHLOROALKYLSILANE CHLORIDES

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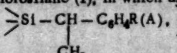
and A. D. Petrov

The possibility of silicoalkylation of various aromatic compounds by chloroalkyltrichlorosilanes and chloroalkyl(alkyl)dichlorosilanes in the presence of $AlCl_3$ or metallic aluminum was demonstrated earlier by us [1,2]. In these investigations it was shown that silicoalkylation products are formed with yields of 30-80%, and a qualitative evaluation of the reactivity of chloroalkyl(alkyl)silane chlorides of various structures was given.

Continuing these investigations, we studied the silicoalkylation of benzene, toluene, and chlorobenzene by dichloroalkylsilane chlorides. The course of these reactions was more complex. Yields of silicoalkylation products in this case proved to be lower (they varied from 3 to 48%), partly owing to a greater degree of resin formation. Furthermore, not only the yields, but also the character of the silicoalkylation products varied in dependence on the nature of both components, as is evident from Table 1, given in the experimental part.

It is of interest to note that in the case of α,α-, β,β-, and α,β-dichloroethyltrichlorosilanes chlorobenzene reacts mainly with both chlorine atoms of the dichloroalkyltrichlorosilane, and with yields about 3 times higher than for benzene. Toluene also reacts with a high yield, but mainly with one chlorine atom; the other chlorine atom is displaced by hydrogen in this case. It is known that toluene is a rather active hydrogen donor. Considerable resin formation is noted in all reactions with toluene. Displacement of chlorine by hydrogen did not occur with dichloromethylsilane chlorides.

In a reaction with α,β-dichloroethyltrichlorosilane (I), in which an aryl radical displaced one chlorine atom, and the second was reduced by hydrogen,  $\geq Si-\underset{CH_3}{\underset{|}{CH}}-C_6H_4R$ (A), $\geq SiCH_2CH_2C_6H_4R$ (B), or a mixture of these could be formed. The same compounds could be formed also from α,α-dichloroethyltrichlorosilane (II), owing to the possibility of intramolecular rearrangement. In the case of β,β-dichloroethyltrichlorosilane (III) migration of the carbonium ion or the chlorine atom to the α-position is excluded on the basis of a critical analysis of all existing literature data on silicoalkylation and the reaction of $AlCl_3$ with chloroalkylsilane chlorides [3].

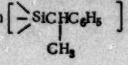
In order to determine the structure of the compounds obtained we turned to the UV absorption spectra. The spectra of the methylated reaction products were obtained with an ISP-22 quartz spectrograph by the photographic method, an Ostroumov-type hydrogen lamp being used as the source of the continuous spectrum. It is known [4] that UV spectra of compounds, in which there is an aliphatic bridge of two carbon atoms (Figure 1a) or one carbon atom (Figure 1b) between the aromatic ring and the silicon atom, exhibit a substantial difference which consists in an approximately 2-fold increase in the intensity of the principal absorption band and the displacement of the entire spectrum by about 5 mμ toward the long-wave region for the second case [cf. the 275 mμ band (Figure 1b) and the 270 mμ band (Figure 1a)]. In compounds of the $\geq SiCH_2C_6H_5$ type substitution of a methyl radical for a hydrogen atom  $\left[\geq Si\underset{CH_3}{\underset{|}{CH}}C_6H_5\right]$ has practically no

TABLE 1

Experiment No.	Silicoalkylating agent	Aromatic compound	Compound obtained	Reaction time (in hr)	Yield based on original chloride (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
1	$Cl_2CHSiCl_3$	C_6H_5Cl	$(ClC_6H_4)_2CHSiCl_3$ Bis(chlorophenyl)methyltrichlorosilane	64	31.2	197—198° (8)	1.5945	1.1343
2	$Cl_2CHSiCl_2CH_3$	C_6H_6	$(C_6H_5)_2CHSiCl_2CH_3$ Bis(phenyl)methylmethyldichlorosilane	40	5.6	134—135 (3)	1.5735	1.1917
3	$Cl_2CHSiCl_2CH_3$	C_6H_5Cl	$(ClC_6H_4)_2CHSiCl_2CH_3$ Bis(chlorophenyl)methylmethyldichlorosilane	40	42.3	196—197 (4.5)	1.5908	1.3383
4	$Cl_2CHSiCl_2CH_3$	$C_6H_5CH_3$	$(CH_3C_6H_4)_2CHSiCl_2CH_3$ Bis(tolyl)methylmethyldichlorosilane	50	4.1	159—163 (4)	1.5639	1.1392
5	$CH_3CCl_2SiCl_3$	C_6H_6	$CH_3C(C_6H_5)_2SiCl_3$ α,α-Diphenylethyltrichlorosilane	12	38	173 (15)	1.5845	1.3111
6	$CH_3CCl_2SiCl_3$	C_6H_5Cl	a) $CH_3CH(C_6H_4Cl)SiCl_3$ α-Chlorophenylethyltrichlorosilane	12	8.7	126—128 (3)	1.5392	1.3528
			b) $CH_3C(C_6H_4Cl)_2SiCl_3$ α,α-Bis(chlorophenyl)ethyltrichlorosilane	12	40	226—227 (5)	1.5985	1.4125
7	$CH_3CCl_2SiCl_3$	$C_6H_5CH_3$	a) $CH_3CH(C_6H_4CH_3)SiCl_3$* α-Tolylethyltrichlorosilane	40	41	96—98 (3)	1.5222	1.2271
			b) $CH_3C(C_6H_4CH_3)_2SiCl_3$ α,α-Ditolylethyltrichlorosilane	40	5.2	156—160 (3)	1.5760	1.2221
8	$Cl_2CHCH_2SiCl_3$	C_6H_6	$(C_6H_5)_2CHCH_2SiCl_3$ β,β-Diphenylethyltrichlorosilane	12	15	168—169 (6.5) M.p. 67—68° (from benzene)	—	—
9	$Cl_2CHCH_2SiCl_3$	C_6H_5Cl	$(ClC_6H_4)_2CHCH_2SiCl_3$ β,β-Bis(chlorophenyl)ethyltrichlorosilane	12	25.8	198—200 (6)	1.5830	1.3954
10	$Cl_2CHCH_2SiCl_3$	$C_6H_5CH_3$	a) $CH_3C_6H_4CH_2CH_2SiCl_3$* β-Tolylethyltrichlorosilane	12	10.7	105—106 (3)	1.5178	1.2139
			b) $(CH_3C_6H_4)_2CHCH_2SiCl_3$ β,β-Ditolylethyltrichlorosilane	12	3.1	173—174 (5) M.p. 53—54° (from benzene)	—	—
11	$ClCH_2CHClSiCl_3$	C_6H_6	a) $C_6H_5CH_2CH_2SiCl_3$ β-Phenylethyltrichlorosilane	13.5	4.2	98—99 (5) **	1.5180	1.2394
			b) $C_6H_5CH_2CH(C_6H_5)SiCl_3$ α,β-Diphenylethyltrichlorosilane	13.5	9.5	162—163 (5) M.p. 60—61° (from benzene)	—	—
12	$ClCH_2CHClSiCl_3$	C_6H_5Cl	a) $ClC_6H_4CH_2CH_2SiCl_3$ α,β-Chlorophenylethyltrichlorosilane	12	4.9	122 (5)	1.5312	1.3459
			b) $ClC_6H_4CH_2CH(C_6H_4Cl)SiCl_3$ α,β-Bis(chlorophenyl)ethyltrichlorosilane	12	27.4	207—208 (5)	1.5833	1.3971
13	$ClCH_2CHClSiCl_3$	$C_6H_5CH_3$	a) $CH_3C_6H_4CH_2CH_2SiCl_3$* β-Tolylethyltrichlorosilane	20	19.6	113—114.5 (7)	1.5178	1.2125
			b) $CH_3C_6H_4CH_2CH(C_6H_4CH_3)SiCl_3$ α,β-Ditolylethyltrichlorosilane	20	5.6	173.5—175 (7)	1.5590	1.2061

* The compound was methylated by means of CH_3MgCl, and the UV spectrum of the reaction product was taken. The properties of the compound are given in Table 2.

** Literature data: b.p. 240.5° (739 mm), n_D^{20} 1.5188, d_4^{20} 1.2395.

TABLE 1 (continued)

	MR_D		Found (in %)				Empirical formula	Calculated (in %)			
	found	calculated	C	H	Si	Cl		C	H	Si	Cl
1	87.71	87.33	41.90, 41.90	2.34, 2.41	7.50, 7.42	46.95, 47.20	$C_{13}H_9Cl_5Si$	42.06	2.54	7.54	47.86
2	77.73	78.02	59.91, 59.88	5.09, 5.04	9.73, 9.70	25.87, 25.94	$C_{14}H_{14}Cl_2Si$	59.78	5.02	9.98	25.22
3	88.35	87.70	48.26, 48.20	3.46, 3.43	8.14, 8.08	39.51, 40.02	$C_{14}H_{12}Cl_4Si$	48.02	3.43	8.02	40.53
4	88.18	87.28	62.82, 62.72	5.97, 5.90	8.51, 8.68	22.18, 22.32	$C_{16}H_{18}Cl_2Si$	62.14	5.87	9.06	22.93
5	82.72	82.28	53.40, 53.50	4.30, 4.36	8.98, 8.98	33.67, 33.45	$C_{14}H_{13}Cl_3Si$	53.25	4.15	8.90	33.70
	62.96	62.41	35.80, 35.72	2.67, 2.44	10.50, 10.52	51.27, 51.20	$C_8H_6Cl_4Si$	35.32	2.28	10.30	52.10
6	92.88	91.96	43.59, 43.62	2.89, 2.86	6.85, 6.94	45.42, 45.68	$C_{14}H_{11}Cl_5Si$	43.69	2.86	7.28	46.17
	62.99	62.67	42.94, 43.02	4.38, 4.40	10.70, 10.62	41.80, 41.55	$C_9H_{11}Cl_3Si$	42.74	4.35	10.74	42.12
7	92.97	91.54	56.55, 56.72	5.20, 5.85	7.66, 7.54	30.10, 30.25	$C_{16}H_{17}Cl_3Si$	56.00	5.00	8.03	30.97
8	—	—	53.52, 53.45	4.32, 4.36	8.98, 8.76	33.10, 33.18	$C_{14}H_{13}Cl_3Si$	53.25	4.15	8.90	33.70
9	92.09	91.96	44.00, 43.96	2.89, 2.86	7.34, 7.28	45.55, 45.75	$C_{14}H_{11}Cl_5Si$	43.69	2.86	7.28	46.17
	62.00	62.67	42.98, 43.00	4.30, 4.28	10.58, 10.55	41.75, 41.62	$C_9H_{11}Cl_3Si$	42.74	4.35	10.79	42.12
10	—	—	55.88, 55.35	5.12, 5.10	8.10, 8.12	31.69, 30.75	$C_{16}H_{17}Cl_3Si$	56.00	5.00	6.03	30.97
	58.54	58.04	—	—	—	—	$C_8H_9Cl_3Si$	—	—	—	—
11	—	—	53.20, 53.10	4.09, 4.10	8.75, 8.83	33.27, 33.12	$C_{14}H_{13}Cl_3Si$	53.25	4.15	8.90	33.70
	62.92	62.88	—	—	—	—	$C_8H_6Cl_4Si$	—	—	—	—
12	91.96	91.96	43.90, 43.86	3.10, 3.05	7.06, 7.10	45.88, 45.98	$C_{14}H_{11}Cl_5Si$	43.69	2.86	7.28	46.17
	63.20	62.87	—	—	—	—	$C_9H_{11}Cl_3Si$	—	—	—	—
13	91.90	91.54	55.81, 55.90	5.10, 5.08	7.94, 8.00	31.16, 31.32	$C_{16}H_{17}Cl_3Si$	56.00	5.00	8.03	30.97

effect on the interaction of the silicon atom and the aromatic ring. UV spectra of compounds of the $>SiCH_2CH_2C_6H_5$ type differ little from those of monoalkylbenzenes.

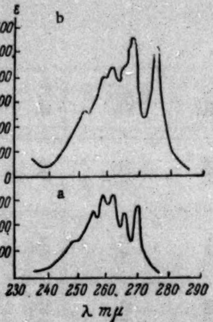


Fig. 1. Ultraviolet spectra of $C_6H_5CH_2CH_2SiR_3$ (a) and $C_6H_5CH_2SiR_3$ (b) in 2,2,4-trimethylpentane solution.

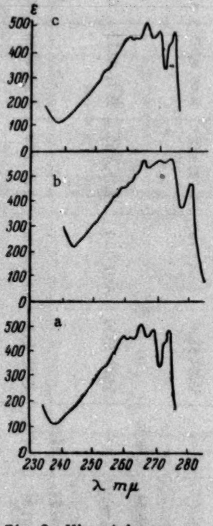


Fig. 2. Ultraviolet spectra of products of the reaction of I (a), II (b), and III (c) with toluene in 2,2,4-trimethylpentane solution.

In Figure 2a, b, c are shown UV spectra of the products of the reaction of toluene with (I), (II), and (III). Spectra a and c are identical. Therefore, in α,β-dichloroethyltrichlorosilane the β-chlorine atom is displaced by an aromatic radical and the α-chlorine atom by hydrogen. The spectrum of the product of reaction of (II) with toluene (Figure 2b) differs from the other two spectra and has the same peculiarities as that in Figure 1b. Therefore, with α,α-dichloroethyltrichlorosilane the reaction takes place, in the main, without rearrangement. However, the complex form of the 267-280 mμ band, two peaks of which (268 and 278 mμ) exactly reproduce the positions of the corresponding peaks of spectra 2a and 2c, and the increased intensity at the point of the principal minimum ($\epsilon = 220$, $\lambda = 247$ mμ instead of the usual $\epsilon \approx 100$) give grounds for assuming that in the formation of type A, insignificant amounts of type B are also formed.

On the basis of comparison of the UV spectra in Figures 2a and 2c, it may be asserted that we have mainly para-isomers in both cases. The presence of the shoulder at 272 mμ suggests that a small amount of the meta-isomer is also formed. In spectrum 2b only one long-wave maximum is observed at about 280 mμ, i.e., displaced exactly 5 mμ with respect to the p-xylene maximum. This, as well as the absence of other bands near this peak, permits the assertion that in this case only the para-isomer is formed.

EXPERIMENTAL

Dichloromethyltrichlorosilane, dichloromethylmethyldichlorosilane, and α,α-, β,β-, and α,β-dichloroethyltrichlorosilanes were prepared by the methods given in [6] and had the following properties: dichloromethyltrichlorosilane, b.p. 144° (750 mm); dichloromethylmethyldichlorosilane, b.p. 148-149° (750 mm); α,α-dichloroethyltrichlorosilane, b.p. 152-153° (750 mm), m.p. 115°; α,β-dichloroethyltrichlorosilane, b.p. 184° (750 mm); β,β-dichloroethyltrichlorosilane, b.p. 173° (750 mm).

The reaction of dichloromethyltrichlorosilane with benzene was described by us earlier [1].

Three standard procedures for conducting the reaction are given. Experimental results are given in Table 1.

1. Bis(chlorophenyl)methyltrichlorosilane. The reaction of dichloromethyltrichlorosilane with chlorobenzene was conducted in a three-neck flask provided

TABLE 2

Original compound	Compound obtained	Yield (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Empirical formula	MR_D found	MR_D calculated
$CH_3CH(C_6H_4CH_3)SiCl_3$ From reaction 7 (Table 1)	$CH_3CH(C_6H_4CH_3)Si(CH_3)_3$ α-Tolylethyltrimethylsilane	70	88—89 (6)	1.4955	0.8756	$C_{12}H_{20}Si$	64.00	63.78
$CH_3C_6H_4CH_2CH_2SiCl_3$ From reaction 10 (Table 1)	$CH_3C_6H_4CH_2CH_2Si(CH_3)_3$ β-Tolylethyltrimethylsilane	73	222—224 (745)	1.4882	0.8640	$C_{12}H_{20}Si$	63.95	63.78
$CH_3C_6H_4CH_2CH_2SiCl_3$ From reaction 13 (Table 1)	$CH_3C_6H_4CH_2CH_2Si(CH_3)_3$ β-Tolylethyltrimethylsilane	78	223—224 (742)	1.4878	0.8637	$C_{12}H_{20}Si$	63.93	63.78

with a stirrer, a thermometer, and a reflux condenser. Into the flask was put 130 g of dichloromethyltrichlorosilane, 224 g of chlorobenzene, and 10 g of $AlCl_3$. The reaction mixture was heated with vigorous stirring at the boiling point of the mixture for 64 hours, after which 20 g of $POCl_3$ was added in order to form the complex $AlCl_3 \cdot POCl_3$. After cooling, the precipitate formed was filtered off, and the filtrate was distilled. On distillation 48 g of dichloromethyltrichlorosilane and 69 g of bis(chlorophenyl)methyltrichlorosilane were isolated; yield, 31.2% based on original and 49.5% based on reacted $Cl_2CHSiCl_3$. All reactions with $Cl_2CHSiCl_3$ and $Cl_2CHSiCl_2CH_3$ were conducted under similar conditions.

2. α,α-Diphenylethyltrichlorosilane. Into the apparatus of Experiment 1, provided with an additional dropping funnel, was placed 40 g of benzene and 3 g of $AlCl_3$. With vigorous stirring a mixture of 46.4 g of α,α-dichloroethyltrichlorosilane and 38 g of benzene was slowly added. The reaction began almost immediately, and HCl was vigorously evolved during the entire time of addition of the mixture. After HCl evolution ceased, the mixture was heated to 70-80° for 10 hours more. Then 6 g of $POCl_3$ and 20 ml of isooctane was added, and after cooling, the precipitate formed was filtered off. On distillation of the filtrate 23.9 g of α,α-diphenylethyltrichlorosilane was isolated. The rest of the reactions with α,α-dichloroethyltrichlorosilane and β,β-dichloroethyltrichlorosilane were conducted under the same conditions.

3. Reaction of α,β-dichloroethyltrichlorosilane and benzene. Into the apparatus of Experiment 1 was placed 35 g of α,β-dichloroethyltrichlorosilane, 78 g of benzene, and 0.3 g of aluminum powder. The mixture was heated to 85° for 3.5 hours, after which vigorous evolution of HCl began. The mixture was heated to 80-90° for 10 hours. Evolution of HCl nearly ceased. On cooling, the reaction product was distilled. One and one-half g of β-phenylethyltrichlorosilane and 4.5 g of α,β-bis(phenyl)ethyltrichlorosilane were obtained. The rest of the reactions with α,β-dichloroethyltrichlorosilane were conducted under the same conditions.

SUMMARY

1. It has been shown that silicoalkylation of benzene, toluene, and chlorobenzene by dichloroethyltrichlorosilanes is accompanied by the reduction by hydrogen of one chlorine atom in the dichloroethyl radical. In the case of benzene and chlorobenzene this is a side reaction, but in the case of toluene it has become the main reaction. In silicoalkylation by means of dichloromethylsilane chlorides reduction is not observed.

2. The UV spectra of a series of the synthesized compounds were taken after methylation of the latter; this made it possible to define the structures of these compounds more exactly.

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Institute of Organic Chemistry of the
Academy of Sciences of the USSR

Received March 11, 1957

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*Original Russian pagination. See C.B. Translation.

**In Russian.

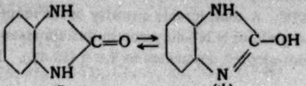
***Russian translation.

CYANOETHYLATION OF BENZIMIDAZOLONE AND MERCAPTOBENZIMIDAZOLE

A. M. Efros

Recently a great number of works [1] on the use of derivatives of urea and thiourea as herbicides and stimulators of vegetable growth have appeared in the literature. Thus it is known that N-4-chlorophenyl-N,N'-dimethylurea is used as a powerful herbicide for combating monocotyledonous weeds [2]. Chlorophenyldimethylurea and N-phenyl-N,N'-dimethylurea [3] are not inferior to this substance with respect to physiological activity. With consumption rates of 9-18 kg per hectare phenyldimethylurea is a herbicide of continuous action. Derivatives of this class of compounds, such as N-3,5-dichloro-4-methoxyphenyl-N,N'-dimethylurea and other compounds [4], are to a greater or lesser degree substances which stimulate vegetable growth, or herbicides.

Cyclic derivatives of urea and thiourea have not yet been studied in this connection. From this point of view benzimidazolone, which was studied in detail by L. S. Efros [5], may be of definite interest as a basis for the synthesis of substances having a herbicidal effect. Thus it has been shown by the investigation of ultraviolet spectra, reactivity, and basicity constants that of the two possible tautomeric forms — orthophenyleneurea (I) and 2-hydroxybenzimidazole (II) — benzimidazolone exists mainly in the first, thus being a cyclic derivative of urea.



(I) (II)

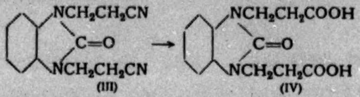
Comparison of the basicity constants and ultraviolet absorption spectra of benzimidazolone, 1,3-dimethylbenzimidazolone, and 2-ethoxybenzimidazole in neutral methanol shows that under ordinary conditions benzimidazolone exists also in the orthophenyleneurea form; benzimidazolone and its 1,3-dimethyl derivative contain a hydroxyl group in position 2, i.e., correspond to form (II), only in a strongly acid medium [6].

Furthermore, it was shown by a whole series of other investigations that in an alkaline medium the alkylation and benzoylation [7,8], of benzimidazolone, as well as its reaction with formaldehyde [9] and its methylation by dimethyl sulfate [10], lead to the formation of N,N'-disubstituted orthophenyleneureas. Neither the cyanoethylation of benzimidazolone nor that of mercaptobenzimidazole is described in the literature.

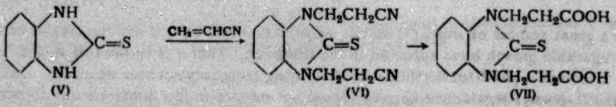
In the present work we decided to study the cyanoethylation of benzimidazolone and mercaptobenzimidazole in the presence of a quaternary base in order to observe the course of the reactions of the given substances with acrylonitrile and to prepare compounds which, from our point of view, must also have physiological activity. The cyanoethylation of benzimidazolone was carried out at a temperature of 40-50° in the presence of triethylbenzylammonium hydroxide as catalyst. In the absence of a catalyst or in the presence of 33% caustic alkali the cyanoethylation of benzimidazolone, as well as that of mercaptobenzimidazole, does not occur. Moreover, if the cyanoethylation is carried out between equimolar quantities of these substances, two acrylonitrile radicals invariably enter into the benzimidazolone or mercaptobenzimidazole molecule.

As a result of the cyanoethylation of benzimidazolone the dinitrile N,N'-dicyanoethylbenzimidazolone (III), m.p. 178-180°, was obtained in good yield.

By hydration of the dinitrile (III) with barium hydroxide in aqueous solution, the barium salt of N,N'-dicarboxyethylbenzimidazolone was obtained; on treatment of this with an equimolar quantity of 0.1 N sulfuric acid the dibasic acid N,N'-dicarboxyethylbenzimidazolone (IV) was obtained in about 80% yield; m.p. 188-189.5°.



The cyanoethylation of mercaptobenzimidazole (V) takes place on longer heating at a higher temperature. On hydration of the dinitrile obtained, N,N'-dicyanoethylbenzimidazolethione (VI), with barium hydroxide and subsequent treatment of the barium salt with 0.1 N sulfuric acid, the dibasic acid, N,N'-dicarboxyethylbenzimidazolethione (VII), m.p. 186-187°, was obtained.



We believe that the cyanoethyl radicals are attached to the nitrogen atoms in the case of both products; however, the exact proof of this requires further investigation.

EXPERIMENTAL

Cyanoethylation of benzimidazolone. Into a three-neck flask, provided with a reflux condenser, a dropping funnel and a thermometer, were put 15 ml of dioxane, 8 g of benzimidazolone, and 0.8 g of triethylbenzylammonium hydroxide; on heating to 40-50°, 14 g (a two-fold excess) of acrylonitrile was gradually added from a dropping funnel. After the beginning of the reaction the reaction mass was heated at 40-50° for 3-4 hours. Thereupon a copious, crystalline precipitate formed, which was filtered off and dried at 105°. The technical product melted at 168-170°. A considerable quantity of the reaction product separated from the mother liquor on evaporation. The yield of N,N'-dicyanoethylbenzimidazole (III), after recrystallization from water, from acetone, and twice from alcohol, amounted to 7.8 g (55.4%). The substance was prepared for the first time.

Found %: C 64.90, 64.58; H 5.40, 5.27; N 23.24, 23.48. $C_{13}H_{12}ON_4$. Calculated %: C 65.00; H 5.00; N 23.3.

Hydrolysis of N,N'-dicyanoethylbenzimidazolone. Two g of (III), 1.4 g of barium hydroxide, and 50 ml of water were put into a two-neck flask provided with a reflux condenser and a thermometer. The solution was boiled for 2-2.5 hours, until ammonia ceased to be evolved. The precipitate was filtered off, the filtrate was saturated by a stream of carbon dioxide, and the resulting barium carbonate precipitate was filtered out of the solution. The solution was then concentrated and treated with an equimolar quantity of 0.1 N sulfuric acid. The dibasic acid dicarboxyethylbenzimidazolone (IV), which was prepared for the first time, was a white, crystalline product readily soluble in alcohol, acetone, or ether. M.p. 188-189.5° after 2-fold recrystallization from water. Yield, 90.3%.

Found %: C 55.55, 55.84; H 5.32, 4.93. M 278, 294 (by potentiometric titration). $C_{13}H_{14}O_5N_2$. Calculated %: C 55.55; H 4.89. M 278.

Cyanoethylation of mercaptobenzimidazole (V). Into a flask with a reflux condenser, a dropping funnel, and a thermometer were put 5 g of mercaptobenzimidazole, 15 ml of dioxane, and 0.5 g of triethylbenzylammonium hydroxide dissolved in 2 ml of ethyl alcohol. The mixture was heated to 50° on a water bath, and 4.5 ml (a twofold excess) of acrylonitrile was gradually added during a 3-hour period. The reaction mixture was heated to 70-75° for 4-5 hours and then poured into 50 ml of water. After 24 hours crystals of N,N'-dicyanoethylbenzimidazolethione (VI) settled out. M.p. 229-230.5° after two recrystallizations from water and then from acetone. Yield, 6 g (70.6%). The product is a white, crystalline substance readily soluble in benzene.

Found %: C 61.16, 61.15; H 4.9, 4.5; N 21.58, 21.26; S 11.87, 11.86. $C_{13}H_{12}N_4S$. Calculated %: C 60.93; H 4.68; N 21.87; S 12.3.

Hydrolysis of N,N'-dicyanoethylbenzimidazolethione (VI). The reaction products were hydrolyzed and worked up under the conditions described above. The dibasic acid obtained, N,N'-dicarboxyethylbenzimidazolethione (VII), is readily soluble in alcohol and in water. The acid was recrystallized twice from acetone and petroleum ether, and it melted at a temperature of 186-187°.

Found: M 302 (by potentiometric titration). $C_{13}H_{14}O_4N_2S$. Calculated: M 294.

SUMMARY

1. N,N'-dicyanoethylbenzimidazolone and N,N'-dicyanoethylbenzimidazolethione have been prepared by cyanoethylation of benzimidazolone and mercaptobenzimidazole, respectively, in the presence of triethylbenzylammonium hydroxide.

2. By hydrolysis of the resulting dinitriles in the presence of barium hydroxide, dicarboxyethylbenzimidazolone and dicarboxyethylbenzimidazolethione were prepared for the first time.

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Leningrad Agricultural Institute

Received December 30, 1956

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* In Russian.

** Original Russian pagination. See C.B. Translation.

CHEMISTRY OF SELENOPHENE

X. SYNTHESIS OF 3-METHYLSELENOPHENE-2-ALDEHYDE AND 2,3- AND 2,4-DIMETHYLSELENOPHENE

Iu. K. Iur'ev, N. K. Sadovaia, and M. A. Gal'bershtam

In the works of Umezawa [1,2] reactions of substitution in the selenophene ring, exemplified by the halogenation, nitration, sulfation, acylation, and mercuration of selenophene, were studied. It follows from these works that with selenophene, as well as its isologs, furan and thiophene, the place of entrance of the second substituent into the ring is determined not only by the nature of the substituent already present and the nature of the second substituent entering the ring, but also to a very considerable degree by the nature of the hetero-atom.

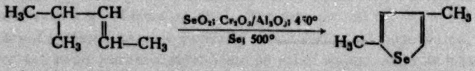
Thus, when a substituent of the first kind, e.g., halogen, is present in position 2 of the selenophene ring, the second substituent (halogen or a nitro group) enters in position 5. If there is a substituent of the second kind (nitro or sulfonyl chloride group) in position 2, the second substituent, e.g., a nitro group, as in the nitration of 2-nitrothiophene, enters positions 4 and 5 in the ring simultaneously to form the isomeric 2,4- and 2,5-dinitroselenophenes, but with predominance of the 2,4-isomer. When a nitro group is present in position 3, the second nitro group enters in position 5.

On conducting the iodination and metalation of the selenophene ring in 3-methylselenophene and 2,4-dimethylselenophene [3], considering that the similarity in structure of selenophene and thiophene must make for close similarity in their chemical properties, we assumed a priori that on replacement of hydrogen by iodine in 3-methylselenophene, 2-iodo-3-methylselenophene is formed; the latter, on subsequent metalation with phenyllithium and carboxylation, gives 3-methylselenophene-2-carboxylic acid. On the same basis we assumed that in the iodination of 2,4-dimethylselenophene replacement of hydrogen by iodine occurs in position 5 of the ring with formation of 5-iodo-2,4-dimethylselenophene, and therefore we assigned the structure of 2,4-dimethylselenophene-5-carboxylic acid to the product of subsequent metalation and carboxylation of the former.

However, it was necessary to prove, firstly, that when there is a methyl group in position 3 of the selenophene ring, halogenation, and also mercuration, actually takes place in position 2, and secondly, that in the case of 2,4-dimethylselenophene these substitution reactions take place in position 5.

In the present work conclusive proofs of the correctness of the orientation of 3-methyl- and 2,4-dimethylselenophene, assumed by us, in the reactions of iodination and mercuration are adduced.

For the preparation of 2,4-dimethylselenophene we used 2-methylpentene-3, which was brought into reaction with selenium dioxide in the presence of chromic oxide on aluminum oxide [4], and also into reaction with metallic selenium [5].



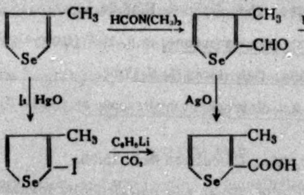
It is evident from the given scheme that on dehydration of 2-methylpentene-3 and ring closure by reaction with selenium [6], either formed from selenium dioxide in the first stage of this process or introduced into the reactor beforehand, only 2,4-dimethylselenophene could be obtained.

For the preparation of 2,3-dimethylselenophene we used 3-methylselenophene; on formylation of the latter by a method developed by one of us [7], we obtained an aldehyde and assigned to it the structure of 3-methylselenophene-2-aldehyde (yield 72%); on reduction of this aldehyde by the usual Kizhner procedure [8] and the method described for the reduction of selenophene-2-aldehyde [7], we accordingly obtained 2,3-dimethylselenophene. Proofs of the correctness of the structures assigned by us to the product of formylation of 3-methylselenophene and the product of subsequent reduction of the aldehyde obtained consist of the following: 1) 2,3-dimethylselenophene differed in its constants (b.p. 159.5-160° at 756 mm, $n^{20}D$ 1.5539, d^{20}_4 1.3734) from 2,4-dimethylselenophene (b.p. 159.5-160° at 746 mm, $n^{20}D$ 1.5498, d^{20}_4 1.3672), described in the present work; 2) the melting point of the chloromercuric derivative of 2,3-dimethylselenophene (~240° with decomp.) sharply differed from that of the chloromercuric derivative of 2,4-dimethylselenophene (155-156°), and a mixture test of them showed a depression (m.p. 145°).

Thus there is no doubt that in the formylation of 3-methylselenophene, 3-methylselenophene-2-aldehyde is obtained, and therefore substitution takes place in position 2.

In order to prove that in the halogenation of 3-methylselenophene halogen replaces hydrogen in position 2, we carried out the oxidation of 3-methylselenophene-2-aldehyde with silver oxide in an alkaline medium and obtained an acid which was 3-methylselenophene-2-carboxylic acid, identical with the acid obtained by us earlier through metalation and subsequent carboxylation of the iodine derivative of 3-methylselenophene [3]: a mixture test-sample of these acids melted without depression.

Thus, in the reactions of halogenation, mercuration, and formylation of 3-methylselenophene, studied by us, displacement of hydrogen situated in position 2 of the selenophene ring takes place.



By reduction of 3-methylselenophene-2-aldehyde with formaldehyde in an alkaline medium we obtained 3-methylselenophene-2-carbinol.

The preparation of isomeric dimethylselenophenes was accomplished through the syntheses of 2,3- and 2,4-dimethylselenophenes, described in the present work.

EXPERIMENTAL

2,4-Dimethylselenophene. a) In accordance with the method of one of us [4], a mixture of 25 g of 2-methylpentene-3 (b.p. 57-58° at 755 mm, $n^{20}D$ 1.3892, d^{20}_4 0.6731) and sublimed selenium dioxide (30 g) was passed over chromic oxide on aluminum oxide in a current of nitrogen at 450° at a space velocity of 0.5 ml of hydrocarbon per ml of catalyst per hour. The catalyzate obtained was washed with water and caustic soda solution and dried with fused caustic potash. On distillation of the reaction product there were isolated 13 g of unchanged 2-methylpentene-3 (52%) and 5.6 g of 2,4-dimethylselenophene (23%, calculated on the basis of reacted hydrocarbon):(b.p. 155-159° at 740 mm, $n^{20}D$ 1.5482, d^{20}_4 1.3639).

b) Fifty g of finely ground selenium was mixed with small pieces of porcelain, put into a silica tube, and heated to 500° [5]. Seventeen g of 2-methylpentene-3 was passed through the tube at a rate of 0.5 ml/min in a slow current of nitrogen. The catalyzate obtained was treated as described above. On distillation of the reaction product there were isolated 8.4 g of unchanged 2-methylpentene-3 (50%) and 3.8 g of 2,4-dimethylselenophene (23.5%, calculated on the basis of reacted hydrocarbon): (b.p. 157-161° at 760 mm, $n^{20}D$ 1.5490, d^{20}_4 1.3680).

The 2,4-dimethylselenophene obtained from a series of experiments was combined and, after distillation in a column (18 theoretical plates), had the following constants:

B.p. 159.5-160° (746 mm), $n^{20}D$ 1.5498, $d^{20}{}_4$ 1.3672, MR_D 37.07. $C_6H_8Se\digamma_2$. Calculated MR_D 37.38.

Found %: C 45.74, 45.81; H 5.14, 5.21. C_6H_8Se. Calculated %: C 45.29; H 5.07.

2,4-Dimethyl-5-chloromercuriselenophene, obtained by the reaction of 2,4-dimethylselenophene with mercuric chloride in aqueous-alcoholic solution in the presence of sodium acetate, melted at 155-156° (from alcohol).

Found %: Hg 50.68, 50.81. $C_6H_7ClHgSe$. Calculated %: Hg 50.84.

3-Methylselenophene-2-aldehyde. Into a three-neck flask with a stirrer, a dropping funnel, and a reflux condenser were put 29.4 g (0.2 mole) of 3-methylselenophene and 18.7 g (0.26 mole) of dimethylformamide, and 39.6 g (0.26 mole) of phosphorus oxychloride was gradually added, the mixture being cooled from time to time with ice water. This was followed by heating for 1 hour at 50-70°, cooling to 20°, and pouring into a mixture of 500 g of ice and 400 g of sodium acetate, with stirring. When the ice melted, the mixture was carefully heated to boiling and cooled, the oil layer was drawn off, the water layer was extracted three times with ether, and the extracts were combined with the oil layer. After drying with anhydrous magnesium sulfate, driving off the ether, and distillation, 25 g (72%) of 3-methylselenophene-2-aldehyde was obtained:

B.p. 111° (12 mm), $n^{20}D$ 1.6198, $d^{20}{}_4$ 1.5602, MR_D 38.93. $C_6H_6OSe\digamma_2$. Calculated MR_D 37.39; EM_D + + 1.54.

Found %: C 41.66, 41.88; H 3.64, 3.66. C_6H_6OSe. Calculated %: C 41.64; H 3.49.

3-Methylselenophene-2-aldehyde semicarbazone: m.p. 202-202.5° (from 50% alcohol).

Found %: N 18.56, 18.44. $C_7H_9ON_3Se$. Calculated %: N 18.26.

3-Methylselenophene-2-aldehyde thiosemicarbazone: m.p. 197° (from alcohol).

Found %: N 16.85, 17.14. $C_7H_9N_3SSe$. Calculated %: N 17.06.

3-Methylselenophene-2-aldehyde 2,4-dinitrophenylhydrazone: m.p. 212-213° (from a mixture of ethyl alcohol and ethyl acetate).

Found %: N 15.82, 15.76. $C_{12}H_{10}O_4N_4Se$. Calculated %: N 15.86.

3-Methylselenophene-2-carboxylic acid. To an aqueous-alcoholic solution of 0.5 g of 3-methylselenophene-2-aldehyde and 1 g of silver nitrate was gradually added 0.3 g of caustic soda in 18 ml of water, with stirring. After standing for a day the silver hydroxide was filtered off, and the filtrate was concentrated, acidified with concentrated sulfuric acid, and extracted with ether. After evaporation of the ether 0.4 g (74%) of 3-methylselenophene-2-carboxylic acid was obtained; m.p. 133-134° (from water). A mixture test with 3-methylselenophene-2-carboxylic acid, obtained from 2-iodo-3-methylselenophene, [3], showed no depression; m.p. 133°.

3-Methylselenophene-2-carbinol. Into a flask with a stirrer, a reflux condenser, a dropping funnel, and a thermometer were put 10.4 g (0.06 mole) of 3-methylselenophene-2-aldehyde, 10 ml of 40% formalin, and 20 ml of anhydrous methyl alcohol. The mixture was heated to 65°, and a solution of 11 g of caustic soda in 10 ml of water was quickly added, the flask being cooled with ice water in order to keep the temperature from exceeding 65°. The mixture was then heated for one-half hour at 60-70°, cooled to 20°, poured on to ice, and extracted three times with benzene; the extracts were washed with 2 N hydrochloric acid and water and dried with anhydrous magnesium sulfate. After driving off the benzene 6.2 g (60%) of 3-methylselenophene-2-carbinol was obtained:

B.p. 116-117° (11 mm), $n^{20}D$ 1.5932, $d^{20}{}_4$ 1.5401, MR_D 38.53. $C_6H_8OSe\digamma_2$. Calculated MR_D 38.90.

Found %: C 41.20, 41.18; H 4.53, 4.62. C_6H_8OSe. Calculated %: C 41.16; H 4.61.

3-Methylselenophene-2-carbinol α-naphthylurethane, obtained by reaction with α-naphthyl isocyanate, melted at 108-109° (from petroleum ether).

Found %: N 3.81, 3.72. $C_{17}H_{15}O_2NSe$. Calculated %: N 4.06.

2,3-Dimethylselenophene. Into a flask with a reflux condenser were put 22 g (0.13 mole) of 3-methylselenophene-2-aldehyde, 25 ml (0.5 mole) of hydrazine hydrate, 15.3 g (0.37 mole) of powdered caustic soda, and 150 ml of diethylene glycol, and the mixture was heated for one-half hour at 130° and then for 1 hour at 180°. The reflux condenser was replaced by a descending one, and everything that passed over up to 180° was distilled off. The distillate obtained was extracted with ether, and the extracts were washed with 2 N hydrochloric acid and dried with calcium chloride. After driving off the solvent and distilling the residue 17.4 g (86%) of 2,3-dimethylselenophene was obtained:

B.p. 159.5-160° (756 mm), $n^{20}D$ 1.5539, d^{20}_4 1.3734, MR_D 37.16. $C_6H_8Se\overline{|}_2$. Calculated MR_D 37.38.

Found %: C 45.42, 45.35; H 5.30, 5.26; Se 49.07, 48.88. C_6H_8Se. Calculated %: C 45.29; H 5.07; Se 49.08.

2,3-Dimethyl-5-chloromercuriselenophene, obtained by the reaction of 2,3-dimethylselenophene with mercuric chloride in aqueous-alcoholic solution in the presence of sodium acetate, melted ~240° with decomposition.

Found %: Hg 50.68, 50.79. $C_6H_7ClHgSe$. Calculated %: Hg 50.84.

A test-sample of a mixture with 2,4-dimethyl-5-chloromercuriselenophene melted at 145°.

Mercuration of 3-methylselenophene. To 1.5 g of 3-methylselenophene, 6.6 ml of alcohol, 3.3 g of sodium acetate, and 6.6 ml of water was added a solution of 3.2 g of mercuric chloride in 40 ml of water with slow agitation, and the mixture was stirred for 6 hours. The white precipitate was filtered off, washed with water, and extracted three times with boiling alcohol (100 ml). On cooling the alcoholic solution 2.8 g (74%) of 3-methyl-2-chloromercuriselenophene was obtained; m.p. 128-129° (from alcohol).

Found %: Hg 52.74, 52.69. $C_5H_5ClHgSe$. Calculated %: Hg 52.76.

The insoluble residue was 3-methyl-2,5-dichloromercuriselenophene; it decomposed on heating.

Found %: Hg 64.82, 64.96. $C_5H_4Cl_2Hg_2Se$. Calculated %: Hg 65.21.

SUMMARY

In the formylation, halogenation, and mercuration of 3-methylselenophene the hydrogen in position 2 of the selenophene ring is displaced.

Formylation of 3-methylselenophene by dimethylformamide leads to 3-methylselenophene-2-aldehyde, which on oxidation gives 3-methylselenophene-2-carboxylic acid and on reduction, 3-methylselenophene-2--carbinol.

Reduction of 3-methylselenophene-2-aldehyde hydrazone leads to 2,3-dimethylselenophene.

The reaction of 2-methylpentene-3 with selenium dioxide in the presence of chromic oxide on aluminum oxide, and also with metallic selenium, leads to 2,4-dimethylselenophene.

With the syntheses of 2,3- and 2,4-dimethylselenophene the preparation of isomeric dimethylselenophenes has been accomplished.

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CONVERSION OF ALLYLBENZENE OVER ALUMINOSILICATE CATALYSTS

I. STUDY OF CONVERSION KINETICS.

K. V. Topchieva, A. I. Pletiushkina and I. A. Zen'kovich

In order to understand the complex processes of conversion of hydrocarbons over aluminosilicates at cracking temperatures, it is first necessary to attempt to study the mechanism of the individual stages of the process under conditions which exclude cracking, as was done in one of the preceding works [1]. In this work the kinetics of isomerization of cyclohexene was studied, and the hypothesis was advanced that the isomerization reaction takes place on active centers of two types — free aluminum oxide and aluminosilicate centers which consist of a chemical compound of the aluminosilicic acid type.

The present investigation is a continuation of work on the study of the mechanism of isomerization reactions of hydrocarbons and a check on the correctness of the expressed point of view on the effect of the two types of active centers on isomerization. For this purpose the kinetics of conversion of an aromatic hydrocarbon with an unsaturated bond in the side-chain — allylbenzene — in the liquid and vapor phases was studied, under conditions which excluded cracking, over aluminosilicate catalysts of varied composition and the initial oxides. The choice of this reaction was favorable also because, as preliminary experiments showed, we were in a position to observe not only the regularities of the isomerization reaction, but also the reactions of di- and polymerization of allylbenzene.

EXPERIMENTAL AND DISCUSSION OF RESULTS

Aluminosilicate catalysts were prepared by mixing freshly precipitated aluminum hydroxide [alumogel] and silica gels [2]. The catalysts were selectively poisoned by the method of exchange adsorption of sodium ions from aqueous sodium acetate solutions [3-5]. The surfaces and structural characteristics of the catalysts obtained were investigated by the adsorption method in a vacuum apparatus of the McBain-balance type, by taking sorption isotherms of methyl alcohol vapor. The surfaces and structural characteristics (volume of micro- and macropores, total porosity) of the poisoned catalyst specimens differed not more than 10% from those of the original catalyst specimens.

Allylbenzene was synthesized according to the method of Tiffeneau [6] by treatment of phenylmagnesium bromide with allyl chloride and purified by distillation over sodium through a rectification column having 40 theoretical plates:

B.p. 156-157° (757 mm), $n^{20}D$ 1.5130, $d^{20}{}_4$ 0.8921, MR_D 39.85; calculated, 39.68.

Literature data [7]: b.p. 156-157° (758 mm), $n^{20}D$ 1.5135, $d^{20}{}_4$ 0.8923, MR_D 39.50.

The study of the kinetics of conversion of allylbenzene over aluminosilicates and the original oxides was carried out in the liquid phase at 157° and in the gas phase over aluminum oxide in the temperature interval 180-250°. The experiments in the liquid phase were conducted in a special, round-bottomed flask provided with a mechanical stirrer, thermostating equipment, and a reflux condenser. The catalyzate obtained was fractionally distilled. The monomeric fraction distilled at normal pressure in the temperature interval 157-176° and was refractometrically analyzed for its allylbenzene and propenylbenzene content [8]. The presence of possible admixtures of other reaction products was checked spectroscopically by taking Raman spectra.* The following fraction distilled at 208-210° (10 mm). Hereafter this fraction will be called the dimer on the basis of data obtained by us in the determination of the composition and structure of the compound.* The amount of the polymer was determined from the residue in the flask; we did not investigate the polymer or determine its structure.

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* E.G. Treshcheva took the Raman spectra, for which we thank her sincerely.

In the study of the kinetics of conversion of allylbenzene in the liquid phase over the original oxides it was noted that on contact of allylbenzene with aluminum oxide, only isomerization of allylbenzene to propenylbenzene occurs. Silica is inactive under the given conditions.

In the study of the kinetics of conversion of allylbenzene over aluminosilicates it was established that under the given conditions the following reactions occur: shifting of the double bond in the side-chain, structural isomerization, and higher degrees of polymerization.

TABLE 1

Quantity of Catalyst, 6.3 cm^3; Duration of Experiment, 4 Hours

Composition of catalyst (in %)**		Products of conversion of allylbenzene (in %)			Total percent of conversion	Composition of catalyst (in %)**		Products of conversion of allylbenzene (in %)			Total percent of conversion
Al_2O_3	SiO_2	propenylbenzene	dimer	polymer		Al_2O_3	SiO_2	propenylbenzene	dimer	polymer	
Temperature 20°						Temperature 100°					
100	0	—	—	—	0	100	0	—	—	—	0
80	20	—	—	—	0	80	20	17	—	—	17
50	50	—	—	—	0	50	50	20	—	—	20
30	70	3	—	—	3	30	70	68	—	—	68
16	84	—	—	—	0	16	84	13	—	—	13
Temperature 50°						Temperature 157°					
100	0	—	—	—	0	100	0	20	—	—	20
80	20	5	—	—	5	80	20	3	60	37	100
50	50	5	—	—	5	50	50	2	52	45	99
30	70	6	—	—	6	30	70	2	78	20	100
16	84	5	—	—	5	16	84	2	60	20	82

In Figures 1-4 is shown the kinetics of conversion of allylbenzene over aluminosilicate catalysts of varied composition; the contact time is plotted along the horizontal axis, and the percent conversion, along the vertical axis.

On comparison of the results obtained with catalysts of compositions 16/84 and 30/70, an analogy is observed in the course of the curves for the yields of reaction products. Thus the curve of propenylbenzene yield over a catalyst of composition 16/84 passes through a pronounced maximum, as does that for a catalyst of composition 30/70 (Figures 1 and 2). The curve of polymer yield has a very pronounced maximum in both cases, while the dimer yield increases with increase of contact time. The overall course of the curves formally corresponds to the course of kinetic curves for consecutive reactions in which the intermediate products are propenylbenzene and a polymer. A different picture is obtained with catalysts containing a high percentage of aluminum oxide in their composition (Figures 3 and 4).

On comparison of the results obtained with catalysts of compositions 50/50 and 80/20, containing aluminum oxide in excess, an analogy is observed in the course of the yield curves of propenylbenzene, the dimer, and the polymer for this pair of catalysts. In this case, however, in contrast to the first pair of catalysts

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* The structure and mechanism of formation of the dimer will be reported in the next article.

** Hereafter, for brevity, the composition of the catalysts will be denoted by a fraction with the percentage of aluminum oxide in the numerator and the percentage of silica in the denominator (16/84, 30/70, 50/50, and 80/20, respectively).

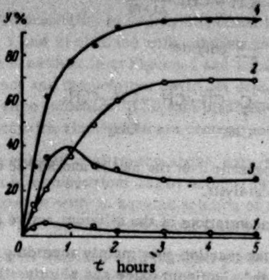


Fig. 1. Kinetics of conversion of allylbenzene over a catalyst of composition 16/84.
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

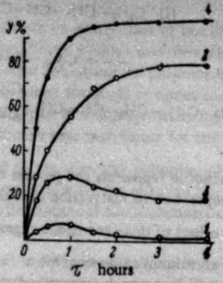


Fig. 2. Kinetics of conversion of allylbenzene over a catalyst of composition 30/70.
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

(16/84 and 30/70), the intermediate reaction products are propenylbenzene and the dimer. This sharp difference in the effect of aluminosilicate catalysts of the stated compositions, as it seems to us, is due to different relative concentrations of active centers (aluminum oxide and aluminosilicate) and the different roles of these centers in isomerization and polymerization. A sharp change in the concentration ratio of the different active centers (aluminum oxide and aluminosilicate in the given case) leads to a change in the course of the kinetic curves, established in the present work.

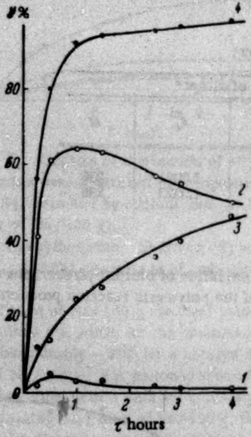


Fig. 3. Kinetics of conversion of allylbenzene over a catalyst of composition 50/50.
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

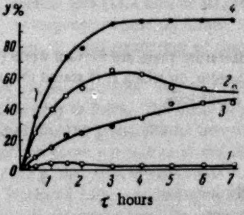
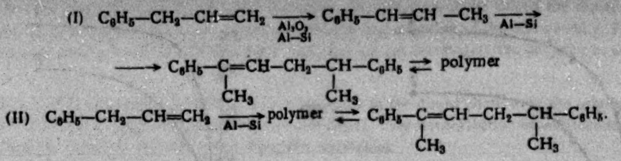


Fig. 4. Kinetics of conversion of allylbenzene over a catalyst of composition 80/20.
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

On the basis of the data obtained on the kinetics of conversion of allylbenzene with aluminosilicate catalysts of varying aluminum oxide content, the following two schemes of the course of the reaction may be given:



$$\text{(I)}\quad C_6H_5-CH_2-CH=CH_2 \xrightarrow[Al-Si]{Al_2O_3} C_6H_5-CH=CH-CH_3 \xrightarrow{Al-Si} C_6H_5-\underset{CH_3}{C}=CH-CH_2-\underset{CH_3}{CH}-C_6H_5 \rightleftarrows \text{polymer}$$

$$\text{(II)}\quad C_6H_5-CH_2-CH=CH_2 \xrightarrow{Al-Si} \text{polymer} \rightleftarrows C_6H_5-\underset{CH_3}{C}=CH-CH_2-\underset{CH_3}{CH}-C_6H_5.$$

The first scheme represents the process of conversion of allylbenzene over the 50/50 and 80/20 catalysts, and the second represents its conversion over the 16/84 and 30/70 catalysts.

The total effect of these reactions depends on the relative concentrations of the different active centers.

When the aluminum oxide content of the catalyst is greater, the reaction goes mainly according to scheme (I); i.e., allylbenzene is isomerized to propenylbenzene on the aluminum oxide and aluminosilicate active centers and then structurally isomerized and converted to the dimer and finally to the polymer on the aluminosilicate centers. If we have a catalyst with a high concentration of aluminosilicate centers and a low content of free aluminum oxide (30/70 and 16/84), the allylbenzene is converted on the aluminosilicate centers to the polymer, which then depolymerizes to form the dimer (scheme II). The occurrence of depolymerization with dimer formation was confirmed by experiments in which the polymer was boiled with the catalyst (Table 2) and by experiments in which the polymer yield was observed to decrease as the temperature increased (Figure 5).

TABLE 2

Experiments in Depolymerization (10 g of Polymer)

Catalyst composition Al_2O_3/SiO_2 (in %)	Quantity of dimer obtained (in %)	Constants of dimer*			
		boiling point	n_D^{20}	d_4^{20}	M
16/84	33	302—304°	1.5686	1.0021	236
30/70	40	302—304	1.5687	1.0022	236

In the literature there are certain works [9-14] on the polymerization of olefin hydrocarbons under the influence of floridin, in which it is stated that depolymerization of the polymeric reaction products occurs under certain conditions.

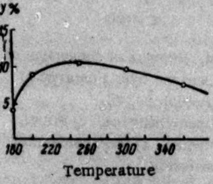


Fig. 5. Dependence of the conversion of allylbenzene to a polymer on the temperature. Catalyst of composition 16/84.

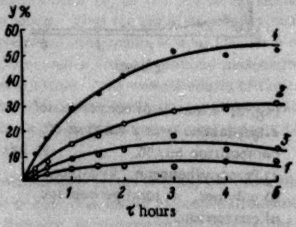


Fig. 6. Kinetics of conversion of allylbenzene over a catalyst of composition 16/84, poisoned by sodium ions (21.8 meq of Na/100 g). 1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

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* The constants of the dimer coincide with those of the dimer obtained from allylbenzene: b.p. 302-304°, $n^{20}D$ 1.5686, $d^{20}{}_4$ 1.0023, M 236.

The possibility of depolymerization in our case becomes obvious on comparison of the kinetic data (Figures 1 and 2) obtained with catalysts containing more aluminosilicate centers than free aluminum oxide ones. It is evident from Figures 1 and 2 that under the given reaction conditions the polymer is an intermediate compound, and the polymer obviously depolymerizes to the dimer, since the yield of dimer increases as the contact time increases. The data obtained indicate that polymerization and depolymerization reactions are associated with aluminosilicate centers, and apparently the latter are alone responsible for the given reactions.

In order to confirm the above, experiments were conducted on the selective poisoning of aluminosilicate catalysts of compositions 16/84 and 50/50 by sodium ions from aqueous solutions of salts [1,3-5]. Treatment of the catalyst with an aqueous solution of sodium salts permits elimination of the aluminosilicate centers from the field of reaction without thereby affecting the free aluminum oxide.

Results obtained with catalysts partially poisoned by sodium ions (Figures 6 – 8) agree with the hypothesis of simultaneous occurrence of the two processes on different centers. From comparison of Figures 6, 7 and 8 with Figures 1 and 2 it is evident that the total percentage of conversion of allylbenzene over a poisoned specimen of composition 16/84, containing 21.8 meq of Na/100 g, was diminished 43-44%; with a specimen containing 41.7 meq of Na/100 g the total percentage of conversion was lowered 80%. The yield of propenylbenzene reached 8%, while for the unpoisoned catalyst it amounted only to 2-3%. The yield of polymer was decreased considerably – 22% for a catalyst containing 21.8 meq of Na/100 g and 32% for one containing 41.7 meq of Na/100 g. For poisoned specimens the maximum on the curve was shifted in the direction of longer contact time. For a catalyst containing 21.8 meq of Na/100 g, the yield of dimer was diminished 38%. For one containing 41.7 meq of Na/100 g, the dimer yield was decreased 63%. An analogous regularity in the decrease of the dimer and polymer yields and the total percentage of conversion was also observed for a catalyst of composition 50/50, poisoned by sodium ions (Figure 8).

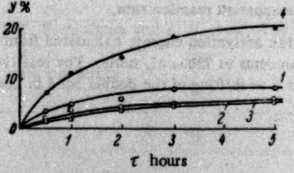

Fig. 7. Kinetics of conversion of allylbenzene over a catalyst of composition 16/84, poisoned by sodium ions (41.7 meq of Na/100 g).
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

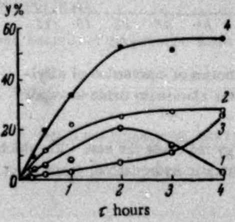

Fig. 8. Kinetics of conversion of allylbenzene over a catalyst of composition 50/50, poisoned by sodium ions (14.4 meq of Na/100 g).
1) Propenylbenzene, 2) dimer, 3) polymer, 4) total percentage of conversion.

From the data given above, it may be concluded that dimerization and polymerization reactions take place only on aluminosilicate centers. Isomerization due to shifting of the double bond in the side-chain takes place both on aluminum oxide centers and on aluminosilicate ones; these reactions go at lower temperatures over aluminosilicate catalysts (Table 1).

On study of the data obtained it becomes obvious that in the case of partial poisoning of the aluminosilicate catalyst the rate of formation of propenylbenzene becomes commensurate with the rates of formation of the dimer and polymer. Over unpoisoned aluminosilicate catalysts the rate of formation of propenylbenzene was quite high; therefore the rate-determining step of the process in this case was the formation of the dimer and polymer.

The study of the kinetics of conversion of allylbenzene in the vapor phase in contact with aluminum oxide was carried out at 180, 200 and 250°. The isomerization of allylbenzene at the stated temperatures over an "alumina-chromia" [alumochrome] catalyst was studied in detail by R.Ia. Levina and co-workers [6,15, 16], and it was shown that allylbenzene is converted to propenylbenzene under these conditions.

As was shown by our experiments, which were conducted in the vapor phase by the method described earlier [1], under the studied conditions, also, allylbenzene is converted only to propenylbenzene; i.e., the reactions of redistribution of hydrogen, dimerization, and polymerization do not take place on contact with aluminum oxide at higher temperatures.

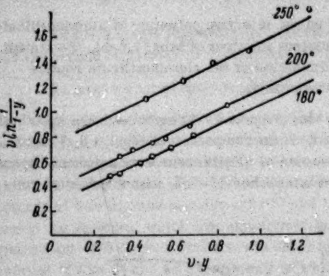

Fig. 9. Kinetics of conversion of allylbenzene over aluminum oxide in vapor phase.

The kinetics of isomerization of allylbenzene in the vapor phase over aluminum oxide (Figure 9), was studied by us, and it was shown that it is described by the equation for a unimolecular heterogeneous-catalytic reaction, in which the reaction products are sorbed more strongly than the molecules of the original substance [17].

$$v \ln \frac{1}{1-y} = \alpha + \beta v y,$$

where v is the rate of input of the original substance, y is the degree of conversion, β is a constant, and α is the apparent reaction rate.

The activation energy, calculated from kinetic data, amounts to 7300 cal/mole. The relatively low activation energy indicates the ease with which isomerization, due to shifting of the double bond in the side-chain of the aromatic hydrocarbon, takes place.

SUMMARY

1. The kinetics of conversion of allylbenzene in the liquid phase over synthetic aluminosilicate catalysts and pure aluminum oxide has been studied.

2. On contact of allylbenzene with aluminosilicate catalysts there occurs not only isomerization due to shifting of the double bond in the side-chain, but also more profound conversions of the original hydrocarbon with formation of the dimer and polymer.

3. Active centers of aluminum oxide in aluminosilicate catalysts lead only to isomerization due to shifting of the double bond in the side-chain. Aluminosilicate centers catalyze the reactions of isomerization, di-, and polymerization. The expressed point of view is confirmed by experiments on the selective poisoning of the active centers of the catalyst.

4. The stepwise mechanism of the conversion of allylbenzene over aluminosilicate catalysts has been established. The difference in the courses of conversion of allylbenzene over catalysts, which differ sharply in their percentage of free aluminum oxide, has been noted.

5. The applicability of the equation for a unimolecular heterogeneous-catalytic reaction in a stream, where the reaction products are sorbed more strongly than the original substances, to the reaction of isomerization of allylbenzene over aluminum oxide in the vapor phase has been shown.

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Received January 28, 1957

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**Transliteration of Russian – Publisher's note.

CONVERSION OF ALLYLBENZENE OVER ALUMINOSILICATE CATALYSTS

II. STRUCTURE AND MECHANISM OF FORMATION OF THE DIMER

K. V. Topchieva, A. I. Pletiushkina and V. A. Tronova

In the preceding work [1] the results of study of the kinetics of conversion of allylbenzene in the liquid phase over aluminum oxide and over aluminosilicate catalysts of diverse compositions were set forth. It was shown that on contact of allylbenzene with aluminum oxide, only isomerization due to shifting of the double bond in the side-chain occurs [2]. Over aluminosilicate catalysts the course of the conversion is far more complex; the reaction products are propenylbenzene, a dimer, and a polymer. The sharp difference between the course of the kinetic curves for catalysts composed of 16% Al_2O_3 and 84% SiO_2, and also 30% Al_2O_3 and 70% SiO_2, and the course of the kinetic curves obtained for catalysts containing a high percentage of aluminum oxide: 50% Al_2O_3 and 50% SiO_2, as well as 80% Al_2O_3 and 20% SiO_2, was also noted. Such a sharp difference in the effects of catalysts of the stated compositions is due to redistribution of the concentration of active centers and their different role in isomerization, dimerization and polymerization.

In the present report are given proofs of the structure and mechanism of formation of the dimer obtained from allylbenzene.

EXPERIMENTAL

The dimer obtained from allylbenzene is an oily, fluorescent liquid:

B.p. 208-210° (10 mm), 302-304° (757 mm), $n^{20}D$ 1.5686, d^{20}_4 1.0023, MR_D 77.60; calculated 78.10; M (cryoscopically) 236, 236.5. $C_{18}H_{20}$; calculated 236.

Found %: C 91.57, 91.58; H 8.28, 8.37. $C_{18}H_{20}$. Calculated %: C 91.47; H 8.53.

At reduced temperatures from -23 to -78° the dimer congeals to the amorphous state. It is readily soluble in organic solvents — benzene, ether, acetone, chloroform, carbon tetrachloride and alcohol; it decolorizes potassium permanganate and bromine water.

The structure of the hydrocarbon was proved by two methods—ozonization and oxidation with potassium permanganate in the cold. After ozonization a ketone and an aldehyde were isolated; the aldehyde was isolated through the dimedon derivative [3]; the ketone, in the form of a semicarbazone, m.p. 198° (from alcohol), and a 2,4-dinitrophenylhydrazone, m.p. 249°.

Literature data for acetophenone [4]: semicarbazone, m.p. 197-198°; 2,4-dinitrophenylhydrazone, m.p. 249-250° [4].

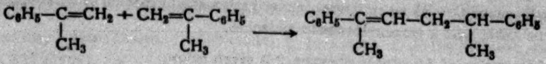
A mixture test of the semicarbazones showed no depression; m.p. 198°.

Thus the ketone isolated on ozonization of the dimer was acetophenone. The structure of the aldehyde obtained (through the dimedon derivative) could not be ascertained.

By oxidation of the dimer with potassium permanganate in the cold two acids were obtained—benzoic acid, m.p. 121° (literature data [5]: m.p. 121°); a mixture test with known benzoic acid gave no depression. The second acid, apparently, was β-phenylbutyric or β-phenylisobutyric acid: m.p. 38°, b.p. 272° (752 mm). Equivalent weight, 164 (calculated for $C_{10}H_{12}O_2$, 164). Literature data [6]: m.p. 38°, b.p. 272°.

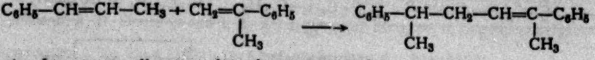
On the basis of the data obtained by us the structure of 2,5-diphenylhexene-2 may be assigned to the unsaturated hydrocarbon. It may be assumed that it is formed as a result of one of the following reactions.

1. Dimerization of α-methylstyrene molecules formed as a result of possible isomerization of propenylbenzene.



$$C_6H_5-\underset{CH_3}{C}=CH_2 + CH_2=\underset{CH_3}{C}-C_6H_5 \longrightarrow C_6H_5-\underset{CH_3}{C}=CH-CH_2-\underset{CH_3}{CH}-C_6H_5$$

2. Condensation of propenylbenzene molecules and already-formed α-methylstyrene molecules.



$$C_6H_5-CH=CH-CH_3 + CH_2=\underset{CH_3}{C}-C_6H_5 \longrightarrow C_6H_5-\underset{CH_3}{CH}-CH_2-CH=\underset{CH_3}{C}-C_6H_5$$

3. Formation from propenylbenzene through a carbonium ion.

Approximate thermodynamic calculations indicate that none of the stated cases are thermodynamically forbidden. The question as to which of the suggested courses is probable could be decided only by conducting counter-syntheses. The results of the counter-syntheses eliminated the first and second courses and permitted us to dwell on the third possible variant, in which the dimer is formed from propenylbenzene by structural isomerization to the styrene form, without formation of the complete α-methylstyrene molecule, with subsequent dimerization.

From literature data [7] it is known that propenylbenzene can be structurally isomerized to α-methylstyrene, and also that in the polymerization of α-methylstyrene over floridin on heating to 200° there are formed, together with polymers, two dimers: a liquid dimer (2,5-diphenylhexene-2), b.p. 302-304°, n^{20}_D 1.5677, d^{20}_4 0.9889, MR_D 77.11 [with composition (in %): C 91.52; H 8.48], and a crystalline dimer, m.p. 52°, to which is assigned the structure of 1,3-dimethyl-2,4-diphenylcyclobutane.

Since the dimer obtained by us and that obtained by Klages [7,8] over floridin are very similar, we considered it necessary to conduct experiments with α-methylstyrene over the aluminosilicate catalysts used in the present work.* The experiments with α-methylstyrene were carried out, over a catalyst of composition 30% Al_2O_3 and 70% SiO_2, in the liquid phase (157°, contact time 1 hour) and in the vapor phase (200°, space velocity equal to unity).

As a result of the experiments it was established that in both the liquid and the vapor phases a crystalline substance with a m.p. of 52°, a b.p. of 302-304°, and an iodine number equal to zero is formed. Obviously this substance is identical with the crystalline dimer obtained by Klages [8].

Thus, it may be considered that the hypothesis that dimerization of already-formed α-methylstyrene leads to production of 2,5-diphenylhexene-2 was not confirmed.

In order to test the second hypothesis a mixture of α-methylstyrene and propenylbenzene (1 : 1) was brought into contact with aluminosilicate.

The propenylbenzene was prepared by passing allylbenzene over aluminum oxide at a rate of 0.15-0.20 ml/min at 200°:

B.p. 174-175°, n^{20}_D 1.5472, d^{20}_4 0.9133. Literature data [2]: b.p. 174.5-175.5°, n^{20}_D 1.5475, d^{20}_4 0.9125.

On passing a mixture of α-methylstyrene and propenylbenzene over a catalyst (16% Al_2O_3 and 84% SiO_2) at 200° at a rate of 0.83 ml/cm³-hour there was obtained a viscous, slightly fluorescent substance which did not contain an unsaturated bond:

B.p. 302-304°, n^{20}_D 1.5684, d^{20}_4 1.0015, MR_D 77.90.

Found %: C 91.27, 91.16; H 8.61, 8.75. M 239, 228. $C_{18}H_{20}$. Calculated %: C 91.47; H 8.53. M 236.

On comparison of the constants of the substance, obtained from a mixture of α-methylstyrene and propenylbenzene, with those of the substance obtained from allylbenzene, it is evident that their constants practically coincide. However, their infrared spectra differ substantially, which does not give grounds for considering the above-described substances identical. Consequently formation of the dimer from propenylbenzene and α-methylstyrene is also improbable.

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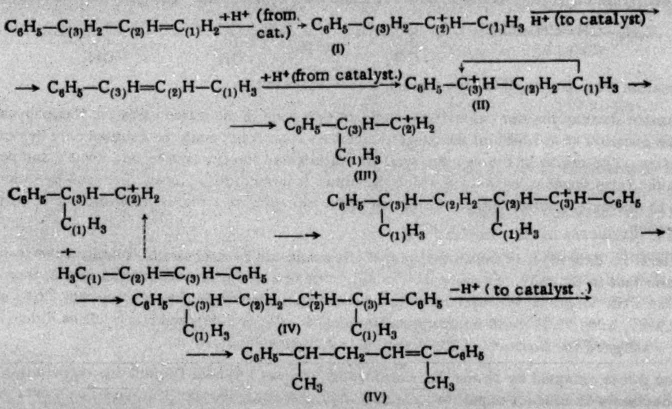
* It must be noted that on investigation of the Raman spectra α-methylstyrene was not found in a single monomer fraction.

Apparently the process of formation of 2,5-diphenylhexene-2 under our conditions goes along the third course—from propenylbenzene through its structural isomerization and formation of a carbonium ion and the subsequent reaction of the latter with a propenylbenzene molecule.

The scheme of formation of 2,5-diphenylhexene-2 is given below.



$$C_6H_5-C_{(3)}H_2-C_{(2)}H=C_{(1)}H_2 \xrightarrow[\text{cat.})]{+H^+\ \text{(from}} \underset{\text{(I)}}{C_6H_5-C_{(3)}H_2-\overset{+}{C}_{(2)}H-C_{(1)}H_3} \xrightarrow{H^+\ \text{(to catalyst)}}$$

$$\longrightarrow C_6H_5-C_{(3)}H=C_{(2)}H-C_{(1)}H_3 \xrightarrow{+H^+\text{(from catalyst.)}} \underset{\text{(II)}}{C_6H_5-\overset{+}{C}_{(3)}H-C_{(2)}H_2-C_{(1)}H_3} \longrightarrow$$

$$\longrightarrow \underset{\text{(III)}}{C_6H_5-\underset{C_{(1)}H_3}{\underset{|}{C_{(3)}H}}-\overset{+}{C}_{(2)}H_2}$$

$$C_6H_5-\underset{C_{(1)}H_3}{\underset{|}{C_{(3)}H}}-\overset{+}{C}_{(2)}H_2 \; + \; H_3C_{(1)}-C_{(2)}H=C_{(3)}H-C_6H_5 \longrightarrow C_6H_5-\underset{C_{(1)}H_3}{\underset{|}{C_{(3)}H}}-C_{(2)}H_2-\underset{C_{(1)}H_3}{\underset{|}{C_{(2)}H}}-\overset{+}{C}_{(3)}H-C_6H_5 \longrightarrow$$

$$\longrightarrow \underset{\text{(IV)}}{C_6H_5-\underset{C_{(1)}H_3}{\underset{|}{C_{(3)}H}}-C_{(2)}H_2-\overset{+}{C}_{(2)}H-\underset{C_{(1)}H_3}{\underset{|}{C_{(3)}H}}-C_6H_5} \xrightarrow{-H^+\ (\text{to catalyst}\ .)}$$

$$\longrightarrow \underset{\text{(IV)}}{C_6H_5-\underset{CH_3}{\underset{|}{CH}}-CH_2-CH=\underset{CH_3}{\underset{|}{C}}-C_6H_5}$$

Under the influence of adsorption forces at the surface of the catalyst, excitation and shifting of the π-bond to one of the carbons of the molecule, C_1, occur. When an active hydrogen ion is present in the structure of the catalyst, and geometrical correspondence exists between the reacting molecule of the substance and the active center of the catalyst, a catalyst proton becomes attached to C_1, this being the more electronegative atom. As a result the carbonium ion (I) is formed. The carbon atom C_2 subsequently becomes attached to a pair of electrons from the adjacent atom C_3, as a result of which the bond between C_3 and the proton is weakened. Owing to this, the catalyst can now regain the proton given off earlier. As a result an electrically neutral molecule is formed, but with the double bond in a new position—propenylbenzene is obtained. Simultaneously the catalyst regains its original properties.

Further, also owing to adsorption forces at the catalyst surface, the π-bond of propenylbenzene may be excited and be shifted to C_2, which, if there is a proton in the catalyst, causes attachment of the proton to C_2. A new carbonium ion (II) is formed. In the carbonium ion thus formed, as is stated in the literature [9,10], there may occur a very simple intramolecular shift of an electron pair together with the methyl group, to which the pair is attached; in this case structural isomerization occurs, as a result of which the carbonium ion (III) is also formed.

The carbonium ion thus formed then reacts with a propenylbenzene molecule through simple addition of the olefin by means of its excess electron pair to C_2, which has a sextet of electrons. The reaction product is a carbonium ion of larger size (IV), in which intramolecular rearrangements and loss of a proton with formation of the dimer, 2,5-diphenylhexene-2, are possible.

It must be noted that with long time of contact of allylbenzene with an aluminosilicate catalyst the formation of 2,5-diphenylhexane together with 2,5-diphenylhexene-2 as a result of the redistribution of hydrogen, is possible.

SUMMARY

1. After contact of allylbenzene with aluminosilicate catalysts (at 157°) the dimer, 2,5-diphenylhexene-2, was isolated and characterized.

2. A scheme for the production of 2,5-diphenylhexene-2 over a catalyst through the formation of a carbonium ion is given.

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Received January 28, 1957

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*Original Russian pagination. See C.B. Translation.

**Russian translation.

SYNTHESIS OF TAGGED DIETHYLAMINOETHYL S^{35}-DIPHENYLHYDROXYTHIOACETATE

S. G. Kuznetsov, Z. I. Bobysheva and E. M. Balonova

In the study of the physiological action of cholinolytic preparations it became necessary to synthesize an active cholinolytic tagged by some radioactive atom. As the objective of synthesis, diethylaminoethyl S-diphenylhydroxythioacetate (II), which, judging from literature data [1], is a considerably more powerful acetylcholine antagonist than diethylaminoethyl S-diphenylthioacetate (thiphen), the synthesis of which with a tagged sulfur atom (S^{35}) is described in the literature [2]. At the same time, it could be expected that the synthesis of diethylaminoethyl S-diphenylhydroxythioacetate with a tagged sulfur atom would be relatively easy to accomplish, using approximately the same scheme as in the case of the synthesis of thiphen.

Diethylaminoethyl S-diphenylhydroxythioacetate was first synthesized [3] through the reaction of diphenylchloroacetyl chloride and diethylaminoethanethiol with subsequent splitting off of the chlorine in the intermediate product (I).

$$(C_6H_5)_2CClCOCl + HSCH_2CH_2N(C_2H_5)_2 \longrightarrow \underset{(I)}{(C_6H_5)_2CClCO—S—CH_2CH_2N(C_2H_5)_2} \xrightarrow{HOH}$$

$$\longrightarrow \underset{(II)}{(C_6H_5)_2C(OH)CO—S—CH_2CH_2N(C_2H_5)_2}$$

For synthesis of the aminothioester with radioactive sulfur we chose this method, modified for use with small quantities of starting materials. BaS^*O_4, containing the sulfur isotope S^{35}, was used as radioactive raw material. In a manner similar to that described for the case of tagged S^{35}-methionine [4], the BaS^*O_4 was reduced by hydrogen at 900-1000° to BaS^*, which was converted to thiourea by treatment with cyanamide and ammonium bicarbonate.

$$BaS^*O_4 \xrightarrow[900—1000°]{H_2} BaS^* \xrightarrow[NH_4HCO_3]{NH_2CN} NH_2—CS^*—NH_2$$

The yield of thiourea, calculated on the basis of BaS^*O_4, even in the case of small quantities of the latter (0.5-0.8 g), was about 95%. Diethylaminoethanethiol was prepared by a method based on the reaction of thiourea with diethyl-β-chloroethylamine and the alkaline hydrolysis of the β-diethylaminoethylisothiourea formed [5].

$$HCl \cdot (C_2H_5)_2NCH_2CH_2Cl + HSC(\cdot NH)NH_2 \longrightarrow$$

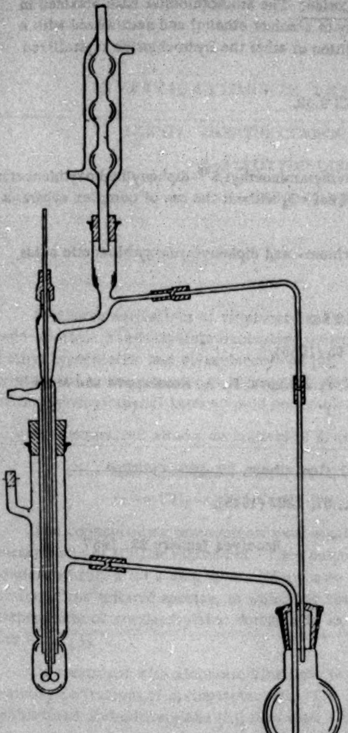
$$\longrightarrow HCl \cdot (C_2H_5)_2NCH_2CH_2—S—C(\cdot NH)NH_2 \cdot HCl \xrightarrow{NaOH}$$

$$\longrightarrow (C_2H_5)_2NCH_2CH_2SH + CO(NH_2)_2.$$

At variance with the cited authors, both stages of the process were carried out not in alcoholic, but in aqueous solution and, furthermore, without isolation of the reaction product. To prevent oxidation of the aminomercaptan its preparation and isolation from solution were carried out in a hydrogen atmosphere in a special liquid-extractor, the construction of which is shown in the diagram.

The yield of diethylaminoethanethiol, calculated on the basis of thiourea, amounted to 70% (in work with not less than 0.7-0.8 g of thiourea). The conversion of the aminomercaptan to the final reaction product—the aminothioester—was carried out in two stages according to the scheme given above [3]. The intermediate reaction product—diethylaminoethyl S-diphenylchlorothioacetate (I)—was isolated as the hydrochloride in the crystalline state. Diethylaminoethyl S-diphenylhydroxythioacetate (II) was initially obtained as the free base, which was then converted to the hydrochloride. The yield of aminothioester hydrochloride, calculated on the basis of diethylaminoethanethiol, amounted to 79% in work with about 5 g of the aminomercaptan and about 30% in work with 1 g of the aminomercaptan. The total yield of the final reaction product in work with small quantities (1.5-2 g) of initial $BaS \bullet O_4$ amounted to 20-22%, calculated on the basis of radioactive raw material. In experiments on a larger scale (8-10 g of $BaS \bullet O_4$), after development of the method of synthesis, the yield of diethylaminoethyl S-diphenylhydroxythioacetate hydrochloride reached 52%.

It should be noted that a sample of the radioactive sulfur-containing substance prepared by the method described in the experimental part differed from an inactive sample by its noticeable reddish color, which vanished when it was dissolved in water or other solvents. In other respects both samples were identical.



Apparatus for preparation and extraction of diethylaminoethanethiol.

EXPERIMENTAL

Barium sulfide and thiourea were prepared from $BaS \bullet O_4$ by methods described in the literature [2,4].

Diethylaminoethanethiol. In a liquid-extractor of 15 ml capacity (see figure), 0.83 g of thiourea and 1.87 g of diethyl-β-chloroethylamine hydrochloride were dissolved in 6.5 ml of water, and the solution was heated to boiling for 6 hours. After cooling to 60° a current of hydrogen was started, and a solution of 0.96 g of caustic soda in 2.7 ml of water was added on expulsion of the air from the system. The mixture was kept in a water bath for 1 hour at 60-70°. On cooling, enough sodium chloride was added to saturate the solution, and the aminomercaptan was extracted with ether for 4 hours. The ether extract was dried with anhydrous sodium sulfate, after which the ether was driven off in a current of hydrogen, and the aminomercaptan was distilled in vacuo from a small flask with a conical bottom. Yield, 1.0 g. B.p. 67.5° at 26 mm.

Diethylaminoethyl S-diphenylchlorothioacetate hydrochloride. To a cooled solution of 1.96 g of diphenylchloroacetyl chloride in 4 ml of dry benzene, placed in a three-neck flask, was gradually added, with stirring, a solution of 1 g of diethylaminoethanethiol in 2 ml of benzene at such a rate as to keep the temperature from exceeding 5°. The dropping funnel was washed with 0.5 ml of benzene, after which the reaction mixture was heated to 60° for 30 minutes and then cooled. The precipitated hydrochloride was filtered out, washed with ether, and dried. Yield, 2.44 g. M.p. 160-162°.

Found %: Cl 17.75, 18.02. $C_{20}H_{25}ONSCl_2$. Calculated %: Cl 17.80.

Diethylaminoethyl S-diphenylhydroxythioacetate. A solution of 2.44 g of diethylaminoethyl S-diphenylchlorothioacetate hydrochloride in 20 ml of water was kept at room temperature for 40 minutes and then at

40° for 10 minutes and was made alkaline with soda solution. The white precipitate of aminothioester base thus formed was filtered out, washed with water, and dried. After crystallization from a mixture of benzene and petroleum ether, 1.53 g of diethylaminoethyl S-diphenylhydroxythioacetate was obtained. M.p. 111-113°.

Found %: N 4.25, 4.37; S 9.42, 9.32. $C_{20}H_{25}O_2NS$. Calculated %: N 4.08; S 9.33.

Diethylaminoethyl S-diphenylhydroxythioacetate hydrochloride. The aminothioester base obtained in the preceding experiment was dissolved in the minimum quantity of absolute ethanol and neutralized with a concentrated alcoholic solution of hydrogen chloride. After addition of ether the hydrochloride crystallized out from the solution. Yield, 1.1 g. M.p. 143-146°.

Found %: Cl 9.24, 9.22. $C_{20}H_{26}NO_2SCl$. Calculated %: Cl 9.33.

SUMMARY

1. A method has been developed for the preparation of diethylaminoethyl S^{35}-diphenylhydroxythioacetate, by which the synthesis may be carried out with small amounts of $BaS^{*}O_4$ without the use of complex apparatus and in a relatively short time.

2. S^{35}-containing diethylaminoethyl S-esters of diphenylchloro- and diphenylhydroxythioacetic acids and their hydrochlorides were prepared for the first time.

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Received January 23, 1957

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*Original Russian pagination. See C.B. Translation.

INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

LXXXIV: DIENYNE COMPOUNDS. I. SYNTHESIS AND PROPERTIES OF β-ALKOXYDIVINYLACETYLENES (ENOL ETHERS OF METHYL VINYLETHYNYL KETONE)

A. A. Petrov

β-Alkoxy derivatives of vinylacetylene were described long ago in the literature [1,2]. An attempt was made to obtain β-ethoxydivinylacetylene through the splitting off of hydrogen chloride from the addition product of ethyl hypochlorite and divinylacetylene [3]. According to analytical data, the substance obtained nearly corresponded to the expected β-ethoxydivinylacetylene; however, it was not pure (it contained 0.5% chlorine), and methylvinylethynyl ketone could not be obtained from it by hydrolysis.

We synthesized alkoxy derivatives of divinylacetylene according to the following scheme:

$$CH_2{=}CH{-}C{\equiv}CMgI + CH_2Br{-}CHBrOR \rightarrow CH_2Br{-}CHOR{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow{KOH}$$

$$\longrightarrow CH_2{=}COR{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow{5\%\ H_2SO_4} CH_3{-}CO{-}C{\equiv}C{-}CH{=}CH_2$$

The corresponding bromoethers were obtained in good yields in the form of colorless oils with the odor characteristic of similar substances. They polymerize on keeping. In the presence of hydroquinone they remain unchanged for a long time. There is no doubt about their structure. It was confirmed by an investigation of the infrared spectra, in which the absorption bands of the triple (4.46 μ) and double (6.24 μ) bonds, characteristic of vinylacetylenic compounds, as well as those of the vinyl group (δ'_{ch} 10.25 and 10.77 μ), were found [4].

On treatment with alcoholic alkali the bromoethers split off hydrogen bromide even in the cold to form β-alkoxy derivatives of divinylacetylene. The latter were colorless, mobile liquids with peculiar odors. Like unsubstituted divinylacetylene [5], they show a high exaltation of the molar refraction (about 2.8).

β-Ethoxydivinylacetylene had a boiling point and refractive index near those of the substance described by A. L. Klebanskii and co-workers [3]; however, it sharply differed from the latter in its specific gravity and chemical properties—susceptibility to polymerization and hydrolysis. A. L. Klebanskii's substance begins to form a film of polymer within a few minutes after isolation, and does not give a ketone on hydrolysis. The β-ethoxydivinylacetylene isolated by us does not polymerize appreciably on keeping for a few days, and on shaking in the cold with 5% sulfuric acid it is easily hydrolyzed with formation of methyl vinylethynyl ketone, which is described in the literature. Thus the substances compared apparently have different structures.

The structures of the β-alkoxy derivatives of divinylacetylene, obtained by us, are determined with certainty by the method of synthesis, and also by hydrolysis data. In the infrared spectra of these substances the band at 4.49 μ corresponded to the triple bond, that at 6.25 μ to the double bond, and those at 10.27 and 10.76 μ to the vinyl group (δ'_{ch}).*

Methyl vinylethynyl ketone, obtained by the hydrolysis of alkoxydivinylacetylenes, has the characteristic, slightly irritating odor of acetylenic ketones. The exaltation of molar refraction, found for it, is considerably higher than that for acetylenic ketones and lower than that for divinylacetylene. On keeping, it turns yellow and polymerizes. It readily forms the well-crystallized 4-nitro- and 2,4-dinitrophenylhydrazones. The latter is described in the literature [6]. Methyl vinylethynyl ketone is hydrogenated in the presence of colloidal palladium to methyl butyl ketone (identified in the form of the crystalline 2,4-dinitrophenylhydrazone).

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* The infrared spectra were taken by G. I. Semenov.

In the infrared spectrum of the ketone a very intense band at 4.51 μ corresponds to the triple bond, one at 6.22 μ (of average intensity) to the double bond, and one at 5.94 μ to the carbonyl group. The deformation bands of the vinyl group are poorly differentiated. The high intensity and sharp decrease in frequency of the band corresponding to the triple bond in comparison with that for acetylenic ketones [7] indicate strong conjugation of the bonds in the molecule of this ketone.

EXPERIMENTAL

Preparation of bromoethers. Into a solution of ethylmagnesium iodide, prepared from 12 g of magnesium, was passed gaseous vinylacetylene (50% excess). The mixture was stirred until the evolution of ethane ceased (about 5 hours). Then, the mixture being cooled with ice, α, β-dibromodiethyl ether (100 g) or α, β-dibromoethyl butyl ether (112 g) was added. After stirring for 3 hours the reaction mixture was poured into a separatory funnel containing a mixture of ice and dilute hydrochloric acid solution. The ether layer was separated and dried over $CaCl_2$, and the ether was distilled off in a water bath. The reaction products were fractionated in vacuo. The first distillation gave a colored product; the second, a colorless one.

Thus 58 g (66% yield, based on the dibromoether) of 6-bromo-5-ethoxyhexen-1-yne-3, 7 g of a lower-boiling fraction, and 5 g of a tarry residue were obtained.

B.p. 68-69° (3 mm), 85-86° (10 mm), d^{20}_4 1.2652, $n^{20}D$ 1.5030, MR_D 47.45; calculated 46.08.

Found %: C 47.65, 47.70; H 5.61, 5.65; Br 39.24. $C_8H_{11}OBr$. Calculated %: C 47.31; H 5.46; Br 39.31.

6-Bromo-5-butoxyhexen-1-yne-3 was obtained in 85% yield.

B.p. 90-91° (3 mm), 111-112° (10 mm), d^{20}_4 1.1784, $n^{20}D$ 1.4870, MR_D 56.44; calculated 55.32.

Found %: C 51.75, 51.79; H 6.85, 7.02; Br 33.65. $C_{10}H_{15}OBr$. Calculated %: C 51.94; H 6.54; Br 34.40.

Preparation of β-alkoxydivinylacetylenes. To a 15% solution of KOH (twofold excess) in methyl alcohol, the bromoether was added through a reflux condenser. A precipitate of potassium bromide immediately formed. The liquid was boiled for 1 hour in a water bath and then was steam distilled. The alkoxydivinylacetylenes were isolated from the distillates by dilution with a saturated $CaCl_2$ solution.

β-Ethoxydivinylacetylene (2-ethoxyhexadien-1,5-yne-3) was obtained in 70% yield.

B.p. 52-52.5° (10 mm), 69-69.5° (15 mm), d^{20}_4 0.8823, $n^{20}D$ 1.5010, MR_D 40.79; calculated 37.85.

Found %: C 78.26, 78.33; H 8.40, 8.45. $C_8H_{10}O$. Calculated %: C 78.65; H 8.25.

β-Butoxydivinylacetylene (2-butoxyhexadien-1,5-yne-3) was obtained in 60% yield.

B.p. 63-64° (3 mm), 81-82° (10 mm), d^{20}_4 0.8764, $n^{20}D$ 1.4928, MR_D 49.79; calculated 47.09.

Found %: C 79.82, 79.71; H 9.59, 9.54. $C_{10}H_{14}O$. Calculated %: C 79.95; H 9.40.

Preparation of methyl vinylethynyl ketone. Five g of ethoxydivinylacetylene was agitated for 12 hours with a 5% solution of H_2SO_4 at room temperature. The mixture obtained was saturated with ammonium sulfate and the upper layer was separated, dried with $CaCl_2$, and distilled in vacuo. One and one-half g (40%) of methyl vinylethynyl ketone (hexen-1-yn-3-one-5) was obtained [6].

B.p. 38-39° (10 mm), 62.5-63° (40 mm), d^{20}_4 0.9264, $n^{15}D$ 1.4890, $n^{20}D$ 1.4842, MR_D 29.07; calculated 27.45.

Hydrazine derivatives were prepared in acetic acid solution; the 4-nitrophenylhydrazone was obtained as microscopic, short, yellow needles, m.p. 120° (from dilute alcohol).

Found %:'Found %: N 18.18, 18.07. $C_{12}H_{11}O_2N_3$. Calculated %: N 18.33.

The 2,4-dinitrophenylhydrazone was obtained as orange rods, m.p. 164° (from a mixture of ethyl acetate and ethyl alcohol).

Found %: N 20.65, 20.65. $C_{12}H_{10}O_4N_4$. Calculated %: N 20.43.

For hydrogenation 0.06 g of the ketone and 1 g of palladium on $CaCO_3$ in 15 ml of methyl alcohol were taken. After absorption of 50 ml of H_2 (765 mm, 18°) the hydrogenation was stopped. To a sample of the solution was added a solution of 2,4-dinitrophenylhydrazine in acetic acid. On dilution of the liquid with water, crystals of methyl butyl ketone 2,4-dinitrophenylhydrazone, m.p. 106-107° (from dilute alcohol), precipitated [8].

Found %: N 20.47. $C_{12}H_{16}O_4N_4$. Calculated %: N 19.99.

SUMMARY

1. The ethyl and butyl ethers of divinylacetylene bromohydrin have been prepared from vinylacetylene and the corresponding α, β-dibromoethers.

2. The dehydrohalogenation products of the above ethers—β-ethoxy- and β-butoxydivinylacetylenes—are described.

3. Hexen-1-yn-3-one-5 has been prepared by the hydrolysis of β-ethoxydivinylacetylene.

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Received March 26, 1957

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*Original Russian pagination. See C.B. Translation.

**Russian translation.

***In Russian.

INVESTIGATION OF ETHERS WITH A DOUBLE BOND IN THE ALLYL POSITION

II. SYNTHESIS OF ETHERS OF α,α,γ,γ-TETRAALKYL-SUBSTITUTED ALLYL ALCOHOLS

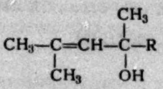
V. I. Pansevich-Koliada and I. F. Osipenko

Aryl-substituted tertiary alcohols very readily form ethers in the presence of a number of acids, acid salts, and hydrolyzed salts [1]. It is still easier to etherify aryl-substituted alcohols containing a double bond in the allyl position by this method [2-5].

It was shown earlier by one of us [6] that 2,4-dimethylhexen-2-ol-4 (II) is also very easily etherified by methyl, ethyl, and allyl alcohols in the presence of a small quantity of dilute sulfuric acid at room temperature.

In connection with the fact that the etherification of tetraalkyl-substituted allyl alcohols has not yet been studied, and also that we found no information in the literature on the ethers obtained thereby, we investigated both the etherification of α,α,γ,γ-tetraalkyl-substituted allyl alcohols and the properties of the ethers, formed thereby, in more detail.

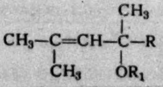
In the present work we carried out the etherification of 2,4-dimethylpenten-2-ol-4 (I), 2,4-dimethylhexen-2-ol-4 (II), 2,4-dimethylhepten-2-ol-4 (III), and 2,4-dimethylocten-2-ol-4 (IV) by primary monatomic alcohols of the aliphatic series.



$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{C}}=CH-\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle OH}{\underset{|}{C}}}}-R$$

(I) $R = CH_3$; (II) $R = C_2H_5$; (III) $R = n\text{-}C_3H_7$; (IV) $R = n\text{-}C_4H_9$

Ethers of the following structure were obtained thereby:

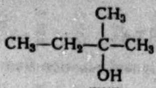


$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{C}}=CH-\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle OR_1}{\underset{|}{C}}}}-R$$

(V) $R = C_2H_5$, $R_1 = n\,C_3H_7$; (VI) $R = C_2H_5$, $R_1 = n\,C_4H_9$; (VII) $R = C_2H_5$, $R_1 = \text{iso-}C_5H_{11}$; (VIII) $R = C_2H_5$, $R_1 = n\text{-}C_6H_{13}$; (IX) $R = n\,C_3H_7$, $R_1 = CH_3$; (X) $R = n\,C_3H_7$, $R_1 = C_2H_5$; (XI) $R = n\,C_3H_7$, $R_1 = n\,C_3H_7$; (XII) $R = n\text{-}C_3H_7$, $R_1 = n\,C_4H_9$; (XIII) $R = n\,C_4H_9$, $R_1 = CH_3$; (XIV) $R = n\,C_4H_9$, $R_1 = C_2H_5$; (XV) $R = n\,C_4H_9$, $R_1 = n\,C_3H_7$; (XVI) $R = n\,C_4H_9$, $R_1 = n\,C_4H_9$.

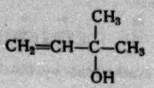
The formation of all the listed ethers takes place extremely readily. On mixing α,α,γ,γ-tetraalkyl-substituted allyl alcohols with primary monatomic alcohols containing a small quantity of dilute sulfuric acid an exothermic reaction takes place, which leads to the formation of the corresponding ether. The reaction is accompanied by a momentary turbidity of the reaction mixture, due to the water which separates out on etherification, and a 1-10° increase in temperature. The yields of ethers formed on etherification by methyl alcohol are usually the highest; the yields usually decrease on transition to higher monatomic alcohols. The structure of the monatomic alcohols has no practical effect on ether formation.

In order to elucidate the effect of the structure of tertiary alcohols on their etherification we conducted experiments on the etherification of 2-methylbutanol-2, (XVII), 2-methylbuten-3-ol-2 (XVIII), 3-methylhexen-5-ol-3 (XIX), and 2,4-dimethylhexanol-4 (XX).



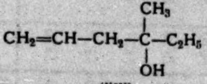
$$CH_3-CH_2-\overset{\displaystyle CH_3}{\underset{\displaystyle OH}{C}}-CH_3$$

(XVII)



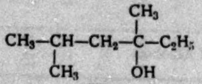
$$CH_2{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle OH}{C}}-CH_3$$

(XVIII)



$$CH_2{=}CH-CH_2-\overset{\displaystyle CH_3}{\underset{\displaystyle OH}{C}}-C_2H_5$$

(XIX)



$$CH_3-\underset{\displaystyle CH_3}{CH}-CH_2-\overset{\displaystyle CH_3}{\underset{\displaystyle OH}{C}}-C_2H_5$$

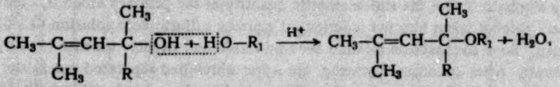
(XX)

These alcohols are tertiary, like the α,α,γ,γ-tetraalkyl-substituted allyl alcohols (I-IV) studied by us. However, in contrast to alcohols (I-IV), alcohols (XVII) and (XX) are saturated, alcohol (XVIII) has no substituents in the γ-position, and alcohol (XIX) has a double bond in the γ, δ-position.

Our attempts to prepare the ethers of alcohols (XVII-XX) with methyl and ethyl alcohols, both under the conditions of etherification of alcohols (I-IV) and on heating at 40-60° for 5-8 hours in the presence of a small quantity of concentrated sulfuric acid, were not successful.

The unusual ease with which the etherification of alcohols (I-IV) takes place is undoubtedly due to the peculiarity of their structure. Tertiary alcohols form ethers more readily than secondary or primary, apparently because the accumulation of radicals on the carbinol carbon atom leads to weakening of the C−O bond. When a vinyl radical gem-substituted by methyl groups is present as a substituent attached to the carbinol carbon atom, this weakening is so great that easy replacement of the hydroxyl group of the tertiary alcohol by alkoxyl is possible.

On the basis of the structural peculiarities of α,α,γ,γ-tetraalkyl-substituted allyl alcohols, their etherification by primary monatomic alcohols in the presence of acid would be expected to take place according to the scheme

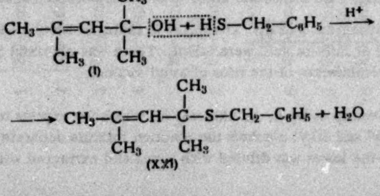


$$CH_3-\underset{\displaystyle CH_3}{C}{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle R}{C}}-\boxed{OH+H}O-R_1 \xrightarrow{H^+} CH_3-\underset{\displaystyle CH_3}{C}{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle R}{C}}-OR_1+H_2O,$$

i.e., as a result of cleavage of the C−O bond of the tertiary alcohol.

This scheme is in conformity with the dehydration of alcohols of this type, which takes place very readily [7], and with the easy displacement of their hydroxyl by halogen on treatment with hydrogen halide [3].

The reaction of 2,4-dimethylpentene-2-ol-4 with benzylmercaptan, which we carried out, is an indirect confirmation of the stated scheme. Under the conditions of etherification of alcohols (I-IV) these substances form the corresponding thioether−2,4-dimethyl-4-benzylthiopentene-2 (XXI) [2,4-dimethylpenten-2-yl-4 benzyl sulfide]−with the same facility. The formation of this thioether is possible only in case of cleavage of the C−O bond of the tertiary alcohol.



$$CH_3-\underset{\displaystyle CH_3}{C}{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-\boxed{OH+H}S-CH_2-C_6H_5 \xrightarrow{H^+}$$

(I)

$$\longrightarrow CH_3-\underset{\displaystyle CH_3}{C}{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-S-CH_2-C_6H_5+H_2O$$

(XXI)

The etherification of the alcohols studied by us apparently takes place through formation of an intermediate carbonium ion, the tendency toward which grows with increase in the number of substituents on the carbinol atom [8]. The mechanism of this reaction is apparently similar to that suggested for the hydrolysis of compounds containing the $O\overset{\bullet}{-}C$ (tert.) bond [9].

EXPERIMENTAL

Tertiary alcohols (I-IV) were synthesized by the Grignard reaction from the corresponding alkyl halides and ketones (Table 1).

TABLE 1

Characteristics of Alcohols

Name of alcohol	RX	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Literature
2,4-dimethylpenten-2-ol-4 (I)	CH_3Cl	58—60° (40)	1.4404	0.8399	35.83	35.58	[10]
2,4-Dimethylhexen-2-ol-4 (II)	C_2H_5Br	44—46 (6—7)	1.4464	0.8515	40.18	40.20	[11]
2,4-Dimethylhepten-2-ol-4 (III)	n-C_3H_7Br	61—62 (7)	1.4480	0.8508	44.74	44.82	[11]
2,4-Dimethylocten-2-ol-4 (IV)	n-C_4H_9Br	74—76 (3)	1.4505	0.8454	49.56	49.44	[11]
2-Methylbutanol-2 (XVII)	C_2H_5I	101 (737)	1.4058	0.8103	26.30	26.81	[12]
2-Methylbuten-3-ol-2 (XVIII)*		96—97 (738)	1.4175	0.8264	26.38	26.35	[13]
3-Methylhexen-5 ol-4 (XIX)	$CH_2{=}CH{-}CH_2Br$	48.8 (22)	1.4370	0.8250	35.42	35.58	[14]
2,5-Dimethylhexanol -4 (XX)	$(CH_3)_2CH{-}CH_2Br$	44.5 (10)	1.4288	0.8288	40.50	40.67	[15]

Preparation of ethers of $\alpha,\alpha,\gamma,\gamma$-tetraalkyl-substituted allyl alcohols. All the ethers were prepared by the following method. Into a three-neck flask, provided with a mechanical stirrer and seal and a thermometer, was put the tertiary alcohol. Twice the stoichiometric quantity of the primary alcohol, containing 5-10% (of the weight of tertiary alcohol taken into the reaction) of aqueous sulfuric acid solution (1 : 5), was poured into one neck with stirring. Soon the reaction mixture became turbid and slightly warmer (1-10°). Stirring was continued for 2-3 hours. After cessation of stirring, the water which had separated out in the course of the reaction was drawn off, and the reaction mixture was diluted with ether, dried with potash,** and distilled in vacuo. The ethers obtained are colorless liquids having pleasant, ethereal odors. All of them are readily soluble in organic solvents and insoluble in water, and quickly decolorize a 1% potassium permanganate solution. They do not contain active hydrogen.

The physical constants of the ethers, obtained by us, and their analyses are given in Table 2.

Ethers of 2,4-dimethylhexen-2-ol-4 (II)

2,4-Dimethyl-4-propoxyhexene-2 (V). To 10 g (0.078 mole) of alcohol (II) was added 16 g (0.214 mole) of propyl alcohol, containing 1 ml of dilute sulfuric acid. There was obtained 5.57 g (41.9%) of the ether.

2,4-Dimethyl-4-butoxyhexene-2 (VI). To 12.5 g (0.0975 mole) of alcohol (II) was added 22.5 g (0.273 mole) of butyl alcohol, containing 1 ml of sulfuric acid. There was obtained 8.22 g of the ether.

2,4-Dimethyl-4-isoamoxyhexene-2 (VII). Ten g (0.078 mole) of alcohol (II), 12.2 g (0.138 mole) of 2-methylbutanol-4, and 0.5 ml of sulfuric acid were taken. There was obtained 8.5 g of a colorless, oily liquid with an odor somewhat reminiscent of the odor of amyl alcohol.

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* Alcohol (XVIII) was kindly given to us by A. A. Akhrem, for which we express to him our sincere gratitude.

** On etherification with methyl and ethyl alcohols the reaction mixture separated into layers. In this case the upper layer was drawn off, and the lower was diluted with water and extracted with ether.

TABLE 2

Characteristics of ethers of $\alpha,\alpha,\gamma,\gamma$-tetraalkyl-substituted allyl alcohols

No.	Name of ether	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Found (%)		Calc. (%)		M	
					found	calculated	C	H	C	H	found	calculated
1	2,4-Dimethyl-4-propoxyhexene-2 (V) $C_{11}H_{22}O$	57—57.9° (7)	1.4328	0.8184	54.19	54.17	77.79	13.18	77.58	13.02	170.3	170.3
2	2,4-Dimethyl-4-butoxyhexene-2 (VI) $C_{12}H_{24}O$	74—74.5 (7)	1.4355	0.8199	58.85	58.79	78.49	13.20	78.19	13.12	182.8	184.4
3	2,4-Dimethyl-4-isoamoxyhexene-2 (VII) $C_{13}H_{26}O$	79.5—80.3 (7)	1.4353	0.8169	63.41	63.41	78.89	13.45	78.72	13.21	198.2	198.3
4	2,4-Dimethyl-4-hexoxyhexene-2 (VIII) $C_{14}H_{28}O$	88—89.5 (7)	1.4401	0.8225	68.06	68.03	78.84	13.44	79.18	13.29	204.8	212.3
5	2,4-Dimethyl-4-methoxyheptene-2 (IX) $C_{10}H_{20}O$	56—56.8 (10)	1.4340	0.8197	49.63	49.55	76.85	13.12	76.86	12.90	149.9	156.2
6	2,4-Dimethyl-4-ethoxyheptene-2 (X) $C_{11}H_{22}O$	61.5—62.5 (10)	1.4344	0.8185	54.24	54.17	77.21	13.02	77.58	13.02	161.2	170.3
7	2,4-Dimethyl-4-propoxyheptene-2 (XI) $C_{12}H_{24}O$	71.5—73 (10)	1.4358	0.8179	58.92	58.79	78.45	13.24	78.19	13.12	184.4	184.4
8	2,4-Dimethyl-4-butoxyheptene-2 (XII) $C_{13}H_{26}O$	85—85.8 (8)	1.4371	0.8185	63.51	63.41	78.50	13.31	78.72	13.21	—	—
9	2,4-Dimethyl-4-methoxyoctene-2 (XIII) $C_{11}H_{22}O$	70.5—71.5 (10)	1.4375	0.8237	54.22	54.17	77.36	13.04	77.58	13.02	164.5	170.3
10	2,4-Dimethyl-4-ethoxyoctene-2 (XIV) $C_{12}H_{24}O$	76.2—76.7 (10)	1.4379	0.8214	58.90	58.79	78.44	13.15	78.19	13.12	180.1	184.4
11	2,4-Dimethyl-4-propoxyoctene-2 (XV) $C_{13}H_{26}O$	89.2—90.2 (10)	1.4389	0.8267	63.20	63.41	78.71	13.04	78.72	13.21	193.1	198.3
12	2,4-Dimethyl-4-butoxyoctene -2 (XVI) $C_{14}H_{28}O$	105—106 (10)	1.4399	0.8222	68.06	68.03	79.14	13.35	79.18	13.29	212.4	212.3

2,4-Dimethyl-4-hexoxyhexene-2 (VIII). Ten g (0.078 mole) of alcohol (II), 16.4 g (0.160 mole) of hexanol-1, and 1 ml of sulfuric acid were taken. There was obtained 8.7 g of the ether in the form of a colorless, immobile liquid.

Ethers of 2,4-dimethylhepten-2-ol-4 (III)

2,4-Dimethyl-4-methoxyheptene-2 (IX). Fifteen g (0.105 mole) of the alcohol, containing 1 ml of sulfuric acid, was taken. There was obtained 12.35 g (78%) of the ether. A colorless, mobile liquid with an agreeable odor.

2,4-Dimethyl-4-ethoxyheptene-2 (X). Fifteen g (0.105 mole) of alcohol (III), 11.82 g (0.257 mole) of ethyl alcohol, and 1 ml of sulfuric acid were taken. There was obtained 10.75 g (59.7%) of the ether.

2,4-Dimethyl-4-propoxyheptene-2 (XI). To 15 g (0.105 mole) of alcohol (III) was added 15 g (0.25 mole) of propyl alcohol, containing 1 ml of sulfuric acid. There was obtained 12.28 g (63.1%) of the ether.

2,4-Dimethyl-4-butoxyheptene-2 (XII). Fifteen g (0.105 mole) of alcohol (III) and 0.213 mole of butyl alcohol, containing 1 ml of sulfuric acid, were taken. There was obtained 10.78 g (51.3%) of the ether.

Ethers of 2,4-dimethylocten-2-ol-4 (IV)

2,4-Dimethyl-4-methoxyoctene-2 (XIII). Fifteen and sixty-two hundredths g (0.1 mole) of alcohol (IV) was etherified with 9.6 g (0.3 mole) of methyl alcohol in the presence of 0.25 ml of sulfuric acid. There was obtained 11.5 g (67.8%) of the ether. A clear, colorless liquid with an agreeable, ethereal odor.

2,4-Dimethyl-4-ethoxyoctene-2 (XIV). To 15.62 g (0.1 mole) of alcohol (IV) was added 13.8 g (0.3 mole) of ethyl alcohol, containing 1.25 ml of sulfuric acid. There was obtained 10.61 g (57.6%) of the ether.

2,4-Dimethyl-4-propoxyoctene-2 (XV). Fifteen and sixty-two hundredths g (0.1 mole) of alcohol (IV), 12 g (0.2 mole) of propyl alcohol, and 0.5 ml of sulfuric acid were taken. There was obtained 9.58 g (48.1%) of the ether.

2,4-Dimethyl-4-butoxyoctene-2 (XVI). Fifteen and sixty-two hundredths g (0.1 mole) of alcohol (IV) was etherified with 14.8 g (0.2 mole) of butyl alcohol in the presence of 1 ml of sulfuric acid. There was obtained 8.64 g (40.7%) of the ether.

Reaction of 2,4-dimethylpenten-2-ol-4 (I) with benzyl mercaptan. Twelve g (0.105 mole) of alcohol (I) was etherified with 6.5 g (0.052 mole) of benzyl mercaptan in the presence of 0.3 ml of sulfuric acid solution. The reaction mixture, which was originally a clear, homogeneous liquid, began to turn opalescent within one-half hour and then grew turbid. After standing for 2 hours, water settled on the walls and bottom of the flask in the form of drops. The odor of benzyl mercaptan was not observed. The water was separated out, and the reaction products were extracted with ether and dried with potash. As a result of distilling twice in vacuo, 4.5 g (42.4%) of 2,4-dimethyl-4-benzylthiopentene-2 was obtained; a colorless liquid with an unpleasant odor which induces headaches and nausea.

B.p. 133-134° (6 mm), $n^{20}D$ 1.5441, d^{20}_4 0.9735, MR_D 71.46; calculated 70.79.[*]

Found %: S 14.35, 14.70. $C_{14}H_{20}S$. Calculated %: S 14.55.

SUMMARY

1. 2,4-Dimethylhexen-2-ol-4, 2,4-dimethylhepten-2-ol-4, and 2,4-dimethylocten-2-ol-4 have been etherified by monatomic primary alcohols of the aliphatic series, and 2,4-dimethylpenten-2-ol-4 has been "etherified" by benzyl mercaptan.

2. It has been established that the presence of a vinyl radical, gem-substituted by methyl groups, on the carbinol carbon makes possible the very easy formation of ethers.

3. The formation of ethers of tetraalkyl-substituted allyl alcohols takes place apparently through displacement of the tertiary-alcohol hydroxyl by an alkoxyl group.

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[*] The atomic refraction of thioether sulfur was taken to be 8.00 [16].

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Received March 14, 1957

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*Russian translation.

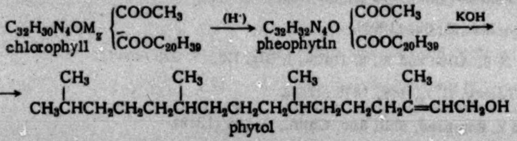
**Original Russian pagination. See C.B. Translation.

***In Russian.

NEW SYNTHESIS OF 2,6,10,14-TETRAMETHYLHEXADECEN--15-OL-14, ISOPHYTOL

I. K. Sarycheva, G. A. Vorob'eva, N. A. Kuznetsova
and N. A. Preobrazhenskii

Present-day published methods of synthesis of tocopherols (vitamins E) and α-phylloquinone (vitamin K_1) are based on the use of 2,6,10,14-tetramethylhexadecen-14-ol-16, phytol, the only source for the derivation of which is vegetable chlorophyll; 1 kg of phytol is obtained from 1 ton of technical chlorophyll [1].

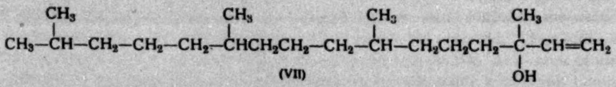


$$\underset{\text{chlorophyll}}{C_{32}H_{30}N_4OMg}\begin{cases}COOCH_3\\COOC_{20}H_{39}\end{cases}\xrightarrow{(H^+)}\underset{\text{pheophytin}}{C_{32}H_{32}N_4O}\begin{cases}COOCH_3\\COOC_{20}H_{39}\end{cases}\xrightarrow{KOH}$$

$$\longrightarrow \underset{\text{phytol}}{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}{=}CHCH_2OH}$$

The known semisyntheses of phytol [2] are based on the use of natural terpene and sesquiterpene alcohols of the aliphatic series; hitherto they have not been widely used, either.

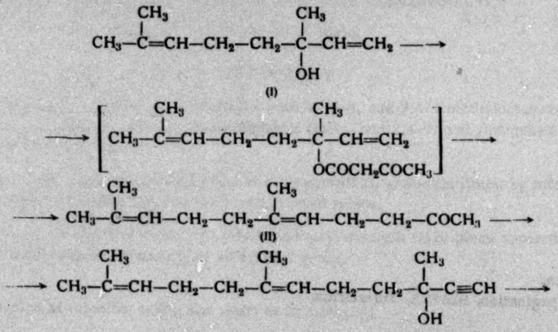
By investigations of the synthesis of tocopherols, α-phylloquinone, and other natural substances it has been established that the compound 2,6,10,14-tetramethylhexadecen-15-ol-14, isophytol (VII), isomeric to phytol, is fully interchangeable with phytol [3].



$$CH_3-\overset{CH_3}{\overset{|}{C}}H-CH_2-CH_2-CH_2-\overset{CH_3}{\overset{|}{C}}HCH_2CH_2-CH_2-\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2-\underset{OH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH{=}CH_2$$

(VII)

In the present work a new full synthesis of isophytol (VII) has been achieved.

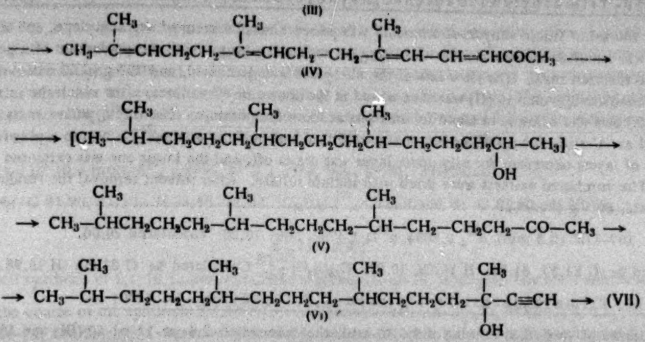


$$CH_3-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-\underset{OH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH{=}CH_2\longrightarrow \quad \text{(I)}$$

$$\longrightarrow\left[CH_3-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-\underset{OCOCH_2COCH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH{=}CH_2\right]\longrightarrow$$

$$\longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-COCH_3\longrightarrow \quad \text{(II)}$$

$$\longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-\overset{CH_3}{\overset{|}{C}}{=}CH-CH_2-CH_2-\underset{OH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-C\equiv CH\longrightarrow$$



$$\longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}=CHCH_2CH_2-\overset{CH_3}{\overset{|}{C}}=CHCH_2-CH_2-\overset{CH_3}{\overset{|}{C}}=CH-CH=CHCOCH_3 \longrightarrow$$

(III) (IV)

$$\longrightarrow [CH_3-\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2\underset{OH}{\underset{|}{C}}H-CH_3] \longrightarrow$$

$$\rightarrow CH_3-\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2-\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2-\overset{CH_3}{\overset{|}{C}}H-CH_2-CH_2CH_2-CO-CH_3 \rightarrow$$

(V)

$$\rightarrow CH_3-\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2\overset{CH_3}{\overset{|}{C}}H-CH_2CH_2CH_2-\overset{CH_3}{\overset{|}{C}}HCH_2CH_2CH_2-\underset{OH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-C\equiv CH \rightarrow (VII)$$

(VI)

The starting material in the synthesis is 2,6-dimethylundecadien-2,6-one-10, geranylacetone (II), which is prepared, starting from synthetic linalool [4] (I), either by means of diketene through the corresponding acetoacetate [5] (Experiment I) or by using acetoacetic ester (Experiment II) and carrying out the reaction without isolation of 2,6-dimethyloctadien-2,7-yl-6 acetoacetate. 2,6-Dimethylundecadien-2,6-one-10 (II) is converted by the action of sodium acetylide dissolved in liquid ammonia to 2,6,10-trimethyldodecadien-2,6-yn-11-ol-10, dehydronerolidol (III), which is then caused to react with acetoacetic ester. In the given case, in contrast to known syntheses of phytol and isophytol (VII) [2], the necessary lengthening of the carbon chain to C_{18} is achieved in one stage. The 2,6,10-trimethylpentadecatetraen-2,6,10,12-one-14 (IV) so synthesized is hydrogenated in the presence of Raney nickel catalyst to 2,6,10-trimethylpentadecanol-14. The latter (omitting the steps of isolation and purification) is oxidized by a mixture of potassium bichromate and sulfuric acid [chrome mixture] in acetic acid solution to 2,6,10-trimethylpentadecanone-14 (V). The latter is further condensed with sodium acetylide; the 2,6,10,14-tetramethylhexadecyn-15-ol-14 (VI) thus obtained is selectively hydrogenated in the presence of Lindlar [6] catalyst to isophytol (VII).

EXPERIMENTAL

1. 2,6-Dimethylundecadien-2,6-one-10, geranylacetone (II)

Experiment I. a) 2,6-Dimethyloctadien-2,7-yl-6 acetoacetate. To 25 g (0.162 mole) of freshly distilled linalool (I) (b.p. 80-80.5° at 10 mm) at 60° in a current of nitrogen was added 0.05 g (0.002 mole) of sodium, and the mixture was kept at 50-55° for 20 minutes. The reaction mixture was then cooled to -5°, and 15.4 g (0.183 mole) of diketene (b.p. 60-61° at 70 mm) was trickled into it in the course of 30 minutes. After standing 24 hours at 0° the mobile, yellow mass that had formed was treated with 15 ml of saturated aqueous sodium carbonate solution and extracted with 300 ml of ether. The extract was dried with sodium sulfate. After the solvent was driven off, the residue was distilled in vacuo. Yield, 31.85 g (82.4%).

B.p. 100-100.5° (1 mm), d^{20}_4 0.9761, $n^{20}D$ 1.4661, MR_D 67.63; calculated 67.58.

Found %: C 70.81, 70.55; H 8.99, 9.24. $C_{14}H_{22}O_3\overline{|}_2$. Calculated %: C 70.53; H 9.31.

b) 2,6-Dimethylundecadien-2,6-one-10, geranylacetone (II). Ten and four-tenths g of 2,6-dimethyloctadien-2,7-yl-6 acetoacetate was heated in a current of nitrogen at 155-160° for 6 hours and then distilled. Yield, 5.75 g (67.8%).

B.p. 83-84° (0.7 mm), d^{20}_4 0.8806, $n^{20}D$ 1.4690, MR_D 61.45; calculated 61.31.

Found %: C 80.17, 80.19; H 11.16, 11.24. $C_{13}H_{22}O\overline{|}_2$. Calculated %: C 80.34; H 11.41.

Experiment II. A mixture of 30 g (0.194 mole) of 2,6-dimethyloctadien-2,7-ol-6 (I) and 88 g (0.68 mole) of acetoacetic ester was heated in a current of nitrogen at 160-170° (about 50 hours). The unreacted acetoacetic ester was then driven off from the reaction mass. The residue was distilled. Yield, 21 g (55.6%).

B.p. 118-120° (7 mm), d^{20}_4 0.8801, $n^{20}D$ 1.4689, MR_D 61.44. $C_{13}H_{22}O\overline{|}_2$. Calculated 61.31.

2. 2,6,10-Trimethyldodecadien-2,6-yn-11-ol-10, dehydronerolidol (III)

Into 750 ml of liquid anhydrous ammonia was passed a rapid current of dry acetylene, and 23 g (1 mole) of sodium was simultaneously added, with stirring, at such a rate as to avoid the production of a persistent blue color in the reaction mass. The flow rate of the acetylene was decreased, and 100 g (0.52 mole) of 2,6-dimethylundecadien-2,6-one-10 (II) was then added in the course of 40 minutes, after which the mixture was stirred for 2 hours and allowed to stand for 16 hours at room temperature. The thick, yellow mass thus formed was treated at -5° with 600 ml of ice water and acidified with sulfuric acid (d^{20}_4 1.395) to a pH of 6.5. Separation of layers occurred; the oily upper layer was drawn off, and the lower one was extracted with 500 ml of ether. The combined extracts were dried with sodium sulfate. After solvent removal the residue was distilled. Yield, 80.5 g (70.9%).

B.p. 107-110° (2.5 mm), d^{20}_4 0.8894, $n^{20}D$ 1.4790, MR_D 70.23; calculated 70.06.

Found %: C 81.87, 81.74; H 10.69, 10.83. $C_{15}H_{24}O|{=}_2|{\equiv}$. Calculated %: C 81.80; H 10.98.

3. 2,6,10-Trimethylpentadecatetraen-2,6,10,12-one-14 (IV)

A mixture of 70 g (0.317 mole) of 2,6,10-trimethyldodecadien-2,6-yn-11-ol-10 (III) and 155 g (1.192 moles) of freshly distilled acetoacetic ester was heated in a current of nitrogen at 165–170° for 55 hours; evolution of carbon dioxide was observed. The unreacted acetoacetic ester was driven off from the reaction mass. The residue was distilled. Yield, 44.93 g (54.3%).

B.p. 110-111° (0.3 mm), 125-127° (0.6 mm), d^{20}_4 0.9114, $n^{20}D$ 1.4951, MR_D 82.85; calculated 83.47.

Found %: C 82.66, 82.79; H 10.65, 10.95. $C_{18}H_{28}O|{=}_4$. Calculated %: C 83.09; H 11.09.

4. 2,6,10-Trimethylpentadecanone-14 (V)

Ninety g of 2,6,10-trimethylpentadecatetraen-2,6,10,12-one-14 (IV) was hydrogenated for 2 hours at 95-100° in a rotary autoclave in the presence of 10 g of Raney nickel catalyst and 100 ml of ethyl alcohol. Initial hydrogen pressure, 90 atm. After cooling to room temperature (45 atm. pressure) the autoclave was emptied, and the catalyst was filtered off and washed with 100 ml of ethyl alcohol. The solvent was distilled off from the combined filtrates. The residue, which amounted to 89 g, had the form of a viscous, light-orange oil. To a mixture of 50 g of the latter and 22.5 g of potassium bichromate in 150 ml of water and 61 g of glacial acetic acid was added 29 ml of sulfuric acid (d^{20}_4 1.395) with stirring in a current of nitrogen. The temperature of the reaction mass thereupon increased spontaneously to 60°. In order to complete the reaction the mixture was heated for 50 minutes at 80-85°. After cooling to room temperature 50 ml of ether was added to it. The upper layer was drawn off, and the lower one was extracted with 200 ml of ether. The ether extract was washed with a saturated aqueous solution of sodium carbonate and dried with sodium sulfate. After the solvent was driven off, the residue was distilled in vacuo. Yield, 34.4 g (69.29%, calculated on the basis of 2,3,6-trimethylpentadecatetraen-2,6,10,12-one-14).

B.p. 110-113° (0.2 mm), d^{20}_4 0.8740, $n^{20}D$ 1.4652, MR_D 84.94; calculated 85.33.

Found %: C 80.21, 80.78; H 13.25, 13.00. $C_{18}H_{36}O$. Calculated %: C 80.52; H 13.52.

5. 2,6,10,14-Tetramethylhexadecyn-15-ol-14 (VI)

To sodium acetylide prepared from 1.83 g (0.08 mole) of sodium and dry acetylene in 100 ml of anhydrous liquid ammonia was added a solution of 10 g (0.037 mole) of 2,6,10-trimethylpentadecanone-14 (V) in 12 ml of anhydrous ether during 15 minutes. The reaction mixture was stirred for 1 hour and allowed to stand for 15 hours at room temperature. The thick, dark-yellow mass thus formed was treated with 30 ml of ice water and was acidified with 15 ml of sulfuric acid (d^{20}_4 1.395) to a pH of 6.5. Separation into layers occurred; the upper layer was drawn off, and the lower one was extracted with 50 ml of ether. The combined extracts were dried with sodium sulfate. After solvent removal the residue was distilled. Yield, 5.9 g (53.6%).

B.p. 119-121° (0.2 mm), d^{20}_4 0.8798, $n^{20}D$ 1.4698, MR_D 93.35; calculated 94.08.

Found %: C 81.30, 81.12; H 12.93, 12.81. $C_{20}H_{38}O|{\equiv}$. Calculated %: C 81.56; H 13.00.

6. 2,6,10,14-Tetramethylhexadecen-15-ol-14, isophytol (VII)

Four g of 2,6,10,14-tetramethylhexadecyn-15-ol-14 (VI) in 40 ml of petroleum ether (b.p. 80-105°) was hydrogenated at 20° in the presence of 0.6 g of palladium catalyst and 0.16 g of quinoline with mechanical agitation. After absorption of 320 ml of hydrogen (105% of the theoretical amount) the hydrogenation was stopped. The catalyst was filtered off and washed with 15 ml of petroleum ether. The combined filtrates were treated with sulfuric acid (d^{20}_4 1.032) and with sodium bicarbonate solution and dried with sodium sulfate. After the solvent was driven off, the residue was distilled. Yield, 3.4 g (84.41%).

B.p. 114-115° (0.4 mm), d^{20}_4 0.8680, $n^{20}D$ 1.4718, MR_D 95.21; calculated 95.61.

Found %: C 81.25, 81.17; H 13.40, 13.62. $C_{20}H_{40}O\Gamma$. Calculated %: C 81.02; H 13.61.

SUMMARY

1. A full synthesis of 2,6,10,14-tetramethylhexadecen-15-ol-14, isophytol, has been achieved.

2. In the course of the synthesis 2,6,10-trimethylpentadecatetraen-2,6,10,12-one-14, 2,6,10-trimethylpentadecanone-14, and 2,6,10,14-tetramethylhexadecyn-15-ol-14 were isolated and characterized.

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Received March 14, 1957

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*In Russian.

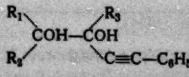
**Original Russian pagination. See C.B. Translation.

INVESTIGATION OF THE CONVERSION OF PINACOLS WITH SUBSTITUTED ACETYLENE RADICALS

XV. ACTION OF MERCURIC SULFATE ON UNSYM. DIMETHYLPHENYL (PHENYLETHYNYL)-AND UNSYM. METHYLDIPHENYL (PHENYLETHYNYL) ETHYLENE GLYCOLS

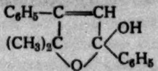
L. A. Pavlova, A. Fabritsy and E. D. Venus-Danilova

In earlier reports by one of us together with A. Fabritsy were given the results of the reactions of unsym. dimethylphenyl (phenylethynyl) ethylene glycol (2-methyl-3,5-diphenylpentyn-4-diol-2,3) (Ia) and unsym. methyldiphenyl (phenylethynyl) ethylene glycol (2-methyl-1,1,4-triphenylbutyn-3-diol-1,2) (Ib) with mercuric chloride and mercuric acetate [1,2], and also that of trimethyl (phenylethynyl) ethylene glycol (2,3-dimethyl-5-phenylpentyn-4-diol-2,3) (Ic) with mercuric chloride [3].

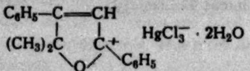


(Ia) $R_1 = R_2 = CH_3$; $R_3 = C_6H_5$.
(Ib) $R_1 = R_2 = C_6H_5$; $R_3 = CH_3$.
(Ic) $R_1 = R_2 = R_3 = CH_3$.

Moreover, it was found that unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia), on reaction with mercuric chloride in alcoholic solution, forms not only the isomerization product of the glycol–5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II)–but also a complex mercury salt of this 2-hydroxydihydrofuran (III), and a mercuration product of the 2-hydroxydihydrofuran (IVa), which was found, on treatment with ammonia, in the form of the symmetrization product [1].



(II)



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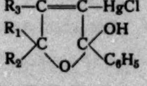
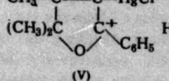


(IVa) $R_1 = R_2 = CH_3$; $R_3 = C_6H_5$
(IVb) $R_1 = R_2 = R_3 = CH_3$.



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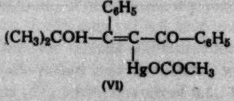


(VI)

On treatment of trimethyl (phenylethynyl) ethylene glycol (Ic) with mercuric chloride the analogous organomercuric compound (IVb) and a complex mercuric salt of the latter (V) are obtained.

In the reaction of mercuric acetate with unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia) the mercuration product (VI), corresponding to the open form of the 2-hydroxydihydrofuran (II) [2], was successfully isolated.

Unsym. methyldiphenyl (phenylethynyl) ethylene glycol (Ib) in the presence of mercuric chloride behaves quite differently, forming the glycol dimer, $C_{46}H_{36}O_2$, with liberation of two molecules of water; with mercuric acetate an addition product of mercuric acetate with the glycol is apparently obtained [3].

In view of the fact that we have hitherto not succeeded in finding hydration products of acetylenic ditertiary α-glycols (Ia, b, c) when using mercury salts (mercuric chloride, bromide, and acetate), we decided to employ mercuric sulfate and to investigate the products of transformation of unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia) and unsym. methyldiphenyl (phenylethynyl) ethylene glycol (Ib) in the presence of this mercury salt.

In this case it was found that unsym. methyldiphenyl (phenylethynyl) ethylene glycol (Ib) is converted on treatment with mercuric sulfate, both in aqueous solution in the presence of a little sulfuric acid and in acetone solution, to the dimer, $C_{46}H_{36}O_2$, described earlier by us [3].

Although the structure of the dimer obtained requires additional proof, it may be assumed that as a result of dehydration and molecular rearrangements 2,5,5-triphenyl-4-vinyldihydrofuran-4,5 is initially formed and then dimerizes like 2,3,3,4-tetramethyl-2-(β,β-dimethylvinyl) dihydrofuran-2,3 [4].

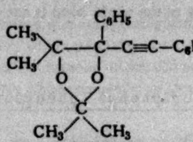
The same dimer was obtained on treatment of glycol (Ib) with mercurous sulfate.

Simultaneously glycol (Ib) was heated for 5 hours with dilute sulfuric acid without addition of mercuric sulfate. In this experiment the glycol was recovered unchanged. This was to be expected, since it is known that unsym. methyldiphenyl (phenylethynyl) ethylene glycol is very stable with respect to sulfuric acid and gives a ketone of the acetylene series only on heating with 40% sulfuric acid [5].

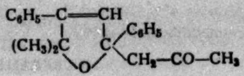
Unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia) was treated with mercuric sulfate under various conditions: in aqueous solution, in aqueous solution in the presence of a little sulfuric acid, and in acetone solution. In the first two experiments the isomerization product of the glycol—5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II)—was obtained. On treatment of the glycol with mercuric sulfate in acetone solution a viscous oil was formed, which gave no sign of the presence of a hydroxyl group and very slowly decolorized a solution of bromine in chloroform, and also potassium permanganate solution; it dissolved in concentrated sulfuric acid with a beautiful, blue fluorescence. The product obtained was successfully purified by distillation in vacuo with a high pumping rate.

The same substance was obtained on treatment of the glycol with mercurous sulfate in acetone solution.

According to the data of elementary analysis and molecular weight, this substance may be either an isopropylidene derivative of the glycol (VII) or a condensation product of hydroxydihydrofuran (II) with acetone—5,5-dimethyl-2,4-diphenyl-2-acetonyldihydrofuran-2,5 (VIII).



(VII)



(VIII)

It was found that the substance obtained is hydrolyzed by 10% sulfuric and 70% acetic acids with the formation of acetone and hydroxydihydrofuran (II). This fact, however, does not yet provide a basis for assigning the structure of the condensation product (VIII) to this substance, since hydroxydihydrofuran (II) may be not the initial product of hydrolysis, but a product formed by isomerization of the glycol under the influence of acid (experiments with 10% sulfuric and 70% acetic acids showed that conversion of the glycol to the hydroxydihydrofuran can take place under these conditions).

In order to solve the problem of the structure of the substance obtained on treatment of an acetone solution of the glycol with mercuric sulfate, we decided to synthesize this substance by another route. Firstly, experiments on the preparation of the isopropylidene derivative (VII) were conducted. For this the acetone solution of the glycol was saturated with hydrogen chloride and allowed to stand for several days [6]. In this case the isopropylidene derivative was not obtained. After neutralizing the solution and distilling off the acetone the original glycol was recovered. Heating of the acetone solution of the glycol with calcined cupric sulfate was also without result.

On the other hand, we attempted to prepare substance (VIII) by condensation of hydroxydihydrofuran (II) with acetone. Heating an acetone solution of hydroxydihydrofuran (II) in a sealed tube, without catalysts and in the presence of calcined cupric sulfate, did not lead to condensation. By heating the acetone solution of hydroxydihydrofuran (II) with mercuric sulfate we obtained a substance which was identical with the product obtained under these conditions from the glycol. On the basis of this experiment the substance obtained from the glycol in acetone solution on treatment with mercuric sulfate may be regarded as 5,5-dimethyl-2,4-diphenyl-2-acetonyl-dihydrofuran-2,5.

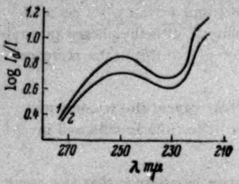


Fig. 1. Ultraviolet absorption spectrum of 5,5-dimethyl-2,4-diphenyl-2-acetonyldihydrofuran-2,5 in ethyl alcohol. 1) Substance obtained from the glycol (Ia) (0.73 x 10^{-4} mole) [0.7310^{-4}]; 2) substance obtained from the hydroxydihydrofuran (II) (0.69 x 10^{-4} mole) [0.6910^{-4}].

In order to confirm the identity of the substances obtained from unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia) and 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II), their absorption spectra in the ultraviolet region* were taken (Fig. 1).

It may be assumed that under the influence of either mercurous or mercuric sulfate the glycol isomerizes to the hydroxydihydrofuran, and the latter condenses with acetone.

It was shown earlier that the hydroxyl group in 2-hydroxydihydrofurans-2,5 has high mobility. This is manifested in reduction [7], in the formation of ketal-type ethers [8], and in condensation with phenylmethylpyrazolone [9]. In this connection the hydroxydihydrofurans are similar to arylcarbinols, for which numerous condensation reactions are known, in particular the condensation of the base of crystal violet (or better, its methyl ether) with acetic and propionic aldehydes [11].

We were unable to prepare carbonyl derivatives of the isolated condensation product, but in the infrared absorption spectrum** of the substance (Fig. 2) there is an intense band with a frequency of 1710 cm^{-1}, characteristic of the carbonyl group [12]. The deformation frequency δ'_{CH} of the $\rangle C=CH$ group, 883 cm^{-1}, is also found in the spectrum; the characteristic frequency of the triple bond is not found.

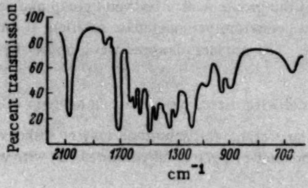


Fig. 2. Infrared spectrum of 5,5-dimethyl-2,4-diphenyl-2-acetonyldihydrofuran-2,5.

EXPERIMENTAL

1. Action of mercuric sulfate on unsym. dimethylphenyl (phenylethynyl) ethylene glycol (Ia)

Experiment I. Two and one-half g of the glycol, 3.5 g of $HgSO_4$, 50 ml of water, and 1.5 ml of H_2SO_4 (sp. gr. 1.83) were heated to boiling for 3 hours. The mixture, which became yellow on heating, was cooled, and the precipitate was filtered off and washed with ether and water. The precipitate weighed 3 g (according to analysis for mercury, the precipitate was the basic salt $HgSO_4 \cdot 2HgO$). From the solution an ether extract was made, which after drying and elimination of ether gave 1.85 g of a clear, rose-colored oil which soon crystallized. After purification the crystalline substance did not give a melting point reduction when mixed with hydroxydihydrofuran (II). From the neutralized aqueous solution 0.5 g more of hydroxydihydrofuran (II) was isolated. The total yield of crude product was 94%.

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* The ultraviolet spectrum was taken with an SF-4 spectrograph.

** The infrared spectrum was taken with an IKS-2 apparatus, having NaCl and LiF prisms, in a 2% solution in CCl_4 with a layer thickness of 1 mm.

Experiment II. Two and one-half g of the glycol, 3.5 g of $HgSO_4$, and 50 ml of water were heated to boiling for 3 hours. At the beginning of the experiment nearly all the material passed into solution, whereupon the entire volume became turbid. After cooling, 2 g of a precipitate was separated out (in its Hg^{++} and SO_4^{--} content the precipitate was similar to the basic salt $HgSO_4 \cdot 2HgO$). An ether-benzene extract was made from the solution, after which the latter was neutralized with soda and treated with ether. After elimination of solvent from the extract made from the acid solution, 2 g of a viscous oil, which crystallized on trituration with benzene, was obtained. The substance obtained did not give a melting point reduction when mixed with hydroxydihydrofuran (II). From the extract obtained from the neutralized solution 0.2 g of a reddish oil, which crystallized after a brief time and also consisted of hydroxydihydrofuran (II), was isolated. The total yield of crude product was 88%.

Experiment III. To a solution of 15 g of the glycol in 200 ml of acetone (dried over $CaCl_2$ and distilled) was added 15 g of $HgSO_4$, and the mixture was heated to boiling, with stirring, for 4 hours. On the following day the precipitate was filtered off and washed with acetone (14.8 g of a substance similar, according to its analysis for mercury, to mercuric sulfate was obtained). From the filtrate, combined with the wash liquids, the acetone was distilled off at a low rate. On concentration of the solution in a distilling flask a small, yellow precipitate was formed, which was subsequently filtered off. The yellow substance (0.4 g)—acicular crystals, m.p. 177-180° (decomp.)—is soluble in ether and in alcohol, is insoluble in benzene and in petroleum ether, and contains mercury. It was not further investigated.

The oil, remaining after separation of the yellow, crystalline substance, was diluted with petroleum ether, freed from precipitated sludge by filtration, washed with water, and dried with sodium sulfate. The viscous liquid obtained after distilling off the petroleum ether, carefully freed from remnants of solvent, was distilled in vacuo. A viscous, light-yellow liquid, b.p. 170-171° (0.22 mm), was obtained. A considerable tarry residue remained in the distilling flask, and a deposit of mercury was found in the side arm. Apparently, a small quantity of the yellow, crystalline product containing mercury was dissolved in the oil and decomposed on distillation in vacuo.

The fraction with a b.p. of 170-171° (0.22 mm) was redistilled. Yield, about 50%.

B.p. 160-161° (0.2 mm), d^{20}_4 1.1120, $n^{20}D$ 1.5728, MR_D 90.65; calculated (VIII) 90.96.

Found %: C 82.69, 82.79; H 6.97, 6.81. M 309. $C_{21}H_{22}O_2$. Calculated %: C 82.35; H 7.19. M 306.

Hydrolysis of the substance obtained. Four g of the product with a b.p. of 160-161° (0.2 mm) was heated with 30 ml of 10% sulfuric acid and 10 ml of alcohol in a water bath for 1.5 hours. The reaction mixture was cooled, partially neutralized with potash, and steam distilled. The distillate was collected in a receiver containing a solution of 2,4-dinitrophenylhydrazine. Immediately there formed a precipitate, m.p. 126°, which did not give a melting point depression when mixed with acetone 2,4-dinitrophenylhydrazone.

The residual mixture was completely neutralized and treated with ether. After the ether was distilled off, an oil was obtained, which partially crystallized. The crystals were separated and purified. There was obtained 2.1 g (60%) of a substance which did not give a melting point depression when mixed with the hydroxydihydrofuran (II). The remainder of the oil (1.4 g) did not crystallize, and after long standing had $n^{20}D$ 1.5740.

Experiment IV. Six g of hydroxydihydrofuran (II), 6 g of $HgSO_4$, and 60 ml of acetone were heated to boiling for 4 hours. The reaction mixture was treated as in Experiment III, whereupon no changes in comparison with Experiment III were observed. The oily product obtained was identical in properties with the substance obtained in Experiment III: it did not react with methylmagnesium iodide, it slowly decolorized a solution of bromine in chloroform, and also potassium permanganate solution, and on addition of a minute quantity of the substance to concentrated sulfuric acid a blue fluorescence appeared. On distillation in vacuo the main part of the substance passed over at 181-182° (0.4 mm); yield, 3.8 g (55%).

d^{20}_4 1.1014, $n^{20}D$ 1.5703, MR_D 91.19; calculated 90.96.

Found %: C 82.52, 82.54; H 7.54, 7.55. M 303.6. $C_{21}H_{22}O_2$. Calculated %: C 82.35; H 7.19. M 306.

The IR spectrum of the substance obtained in Experiment IV, taken in the 1590-1730 cm^{-1} region, coincides well with that of the substance obtained in Experiment III (Fig. 2).

Experiment V was conducted with a solution of 10 g of the glycol in 125 ml of acetone, to which was added 10 g of Hg_2SO_4, under the conditions of Experiment III. From the reaction products 9.6 g of a grayish precipitate of the mercury salt was obtained. The filtrate was treated as in Experiment III. On concentration of the filtrate separation of a small quantity of a yellow substance containing mercury was again observed. The oil obtained was distilled in vacuo: 1st fraction, 150-154° (0.24 mm), $n^{20}D$ 1.5711; 2nd fraction, 154-163° (0.24 mm), $n^{20}D$ 1.5721.

There was a considerable gray deposit in the side arm and a rather large tarry residue in the bulb.

The 2nd fraction was redistilled. The main mass passed over at 166-172° (0.3 mm), $n^{20}D$ 1.5730. The part of this distillate having a b.p. of 169-170° (0.3 mm), was withdrawn for analysis.

B.p. 169-170° (0.3 mm), d^{20}_4 1.1056, $n^{20}D$ 1.5721, MR_D 91.08; calculated 90.96.

Found %: C 82.65, 82.51; H 7.39, 7.36. M 304. $C_{21}H_{22}O_2$. Calculated %: C 82.35; H 7.19. M 306.

II. Action of mercuric sulfate on unsym. methyldiphenyl (phenylethynyl) ethylene glycol (Ib)

Experiment I. A mixture of 3 g of the glycol (m.p. 120-121°), 2.9 g of $HgSO_4$, and 60 ml of water, to which had been added 1.5 ml of H_2SO_4 (sp. gr. 1.83), was heated to boiling for 2 hours. Next day the reaction mixture had acquired an orange color, and a benzene extract of it gave 2 g of reddish, tarry product, which was dissolved several times in ether and precipitated with alcohol. From the alcoholic-ethereal mixture a yellowish, amorphous substance, m.p. 108-117°, which did not contain mercury, separated out.

Found %: C 88.80, 88.78; H 5.98, 6.00. M 624. $C_{46}H_{36}O_2$. Calculated %: C 89.03; H 5.83. M 620.

Experiment II. Four g of the glycol, 3.7 g of $HgSO_4$, and 65 ml of acetone were heated to boiling for 3 hours. After distilling off the acetone a dark oil was obtained, which was dissolved in ether. On addition of a large amount of alcohol to the ether solution a yellowish, amorphous powder separated out, which was identical with the product obtained in Experiment I and that obtained earlier on treatment of glycol (Ib) with mercuric chloride [3].

Experiment III. Two g of glycol (Ib), 1.9 g of Hg_2SO_4, 40 ml of water, and 1 ml of H_2SO_4 (sp. gr. 1.83) were heated to boiling for 5 hours with stirring. At first the glycol floated on the surface, while the Hg_2SO_4 lay chiefly at the bottom. Gradually an oily substance appeared, which enveloped the mercury salt, and on the stirrer a lump formed, which hardened on cooling. The hard mass was agitated with ether. Thereupon the organic part passed into solution, and the Hg_2SO_4 (1.75 g) formed a precipitate. Isolation and purification were carried out as in Experiment I. There was isolated 1.7 g (82%) of an amorphous substance, melting in the interval 107-119°, which was quite similar to the dimer obtained on treatment of glycol (Ib) with $HgSO_4$ or $HgCl_2$ [3].

Found %: C 89.27; H 5.53. M 607. $C_{46}H_{36}O_2$. Calculated %: C 89.03; H 5.89. M 620.

The same substance was also obtained on treatment of glycol (Ib) with Hg_2SO_4 in the presence of acetone.

SUMMARY

1. It has been shown that unsym. dimethylphenyl (phenylethynyl) ethylene glycol (2-methyl-3,5-diphenylpentyn-4-diol-2,3) is converted to 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 on treatment with mercuric sulfate.

2. It has been established that in the presence of mercuric sulfate 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 condenses with acetone, forming 5,5-dimethyl-2,4-diphenyl-2-acetonyldihydrofuran-2,5, which is not described in the literature.

3. Unsym. methyldiphenyl (phenylethynyl) ethylene glycol forms a dimer of uncertain structure on treatment with mercuric sulfate.

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Received January 23, 1957

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* Original Russian pagination. See C.B. Translation.

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INVESTIGATION IN THE FIELD OF VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

I. HYDRATION OF VINYLACETYLENE TO METHYL VINYL KETONE

Iu. A. Gorin and L. P. Bogdanova

The addition of water to vinylacetylene in the liquid phase under the influence of mercury salts to form methyl vinyl ketone was first accomplished by J. Nieuwland [1]. This reaction was later studied by a number of authors [2-5]. I. N. Nazarov [6] carried out the hydration of vinylacetylene in alcoholic solutions, and he thus obtained methyl β-alkoxyethyl ketones in 55-90% yields, calculated on the basis of the vinylacetylene taken. Other methods of obtaining methyl vinyl ketone are also known [7-9], but the method of preparation of the latter by hydration of commercial vinylacetylene is the simplest.

The reaction between water and acetylene may also be carried out in the vapor phase under the influence of various solid catalysts. There are a number of patents, journal articles, and reviews [10] in which the use of oxides and various salts of zinc, copper, and cadmium (phosphates, tungstates, and other salts of these metals), as well as mixtures of certain of these with phosphoric acid, as catalysts for this process, is described. In many cases these catalysts are deposited on carriers, among which activated charcoal, calcium phosphate, "cuprene", and a number of other substances are mentioned. The employment of such catalysts for the process of hydration of acetylene to aldehyde makes it possible to abandon the use of mercury salts, which are toxic substances.

If the problem of vapor-phase hydration of acetylene has received a relatively great amount of attention, no one has been engaged in the study of hydration reactions of acetylene derivatives over solid catalysts, although the investigation of these processes may have not only theoretical interest, but also practical importance as one of the ways of obtaining ketones useful as starting materials for various organic syntheses.

Methyl vinyl ketone—a product of the hydration of vinylacetylene—may be used for various syntheses [11-13], including one of the steps in the synthesis of vitamin A [14,15]. In the latter case the use of methyl vinyl ketone prepared from vinylacetylene by treatment with mercury salts is undesirable, since traces of mercury may remain in the final product and may pass into the human organism. Obviously methyl vinyl ketone obtained through the vapor-phase hydration of vinylacetylene over catalysts not containing mercury must be free from the stated faults.

In the present work it is shown that solid catalysts such as zinc oxide, cadmium tungstate, cadmium-calcium-phosphate catalyst, and tungsten trioxide may be used for the successful hydration of vinylacetylene to methyl vinyl ketone in the gas phase. In carrying out the process the hydrocarbon is diluted with 10 times its volume of steam. The methyl vinyl ketone thus formed is found among the reaction products, partly in the aqueous solution and partly in the upper oil layer, from which it may be recovered by rectification. Together with methyl vinyl ketone, a small quantity of vinylacetylene polymerization products (mainly the trimer, apparently) and a dimer of methyl vinyl ketone (2-acetyl-6-methyl-2,3-dihydropyran) are obtained.

The results of the effect of the temperature and space velocity of the vinylacetylene on the process of hydration of the latter in the presence of various catalysts are given in the table. A comparative evaluation of the activity and selectivity of action of the catalysts investigated may be made by comparing the results of experiments 1, 7, 12, and 17, which were carried out under the same conditions of space velocity and dilution of the hydrocarbon with steam (1 : 10) and in which about the same degree of conversion of vinylacetylene was obtained.

TABLE

Effect of Temperature and Space Velocity on the Process of Hydration of Vinylacetylene Over Various Catalysts (Average Data of Three Experiments)

Experiment No.	Name of Catalyst	Temperature of experiment	Space vel. vinylacetylene (1/1 cat./hr)	Deg. conversion methylvinylacetylene (in %)	Methyl vinyl ketone on basis of reacted vinylacetylene (in %)	Productivity with respect to methyl vinyl ketone (g/1 cat./hr)
1	Cadmium tungstate	325°	100	31.8	87.0	85
2		350	100	50.5	76.0	121
3		375	100	59.0	73.2	133
4		375	150	35.0	81.0	131
5		400	150	57.5	70.0	183
6	Cadmium phosphate on calcium phosphate $\frac{CdO + CaO}{P_2O_5} = 2.88$	350	100	24.1	78.0	62
7		375	100	32.8	72.5	79
8		400	100	39.1	52.5	63
9		350	150	19.7	83.0	80
10		375	150	24.3	80.0	91
11	Tungsten trioxide	350	100	27.6	74.5	62
12		375	100	38.8	69.0	81
13		400	100	52.2	65.5	103
14		350	70	48.7	71.5	76
15	Zinc oxide	375	100	14.3	91.0	38
16		400	100	17.7	84.5	36
17		425	100	32.4	75.5	78
18		400	70	20.4	81.6	41

It follows from the data of the table that cadmium tungstate has the greatest catalytic activity and selectivity with respect to yield of methyl vinyl ketone. For equal space velocities of vinylacetylene, the same degree of conversion of the latter is attained with this catalyst at a lower temperature than with the other catalysts. Lower results were obtained with a cadmium-calcium-phosphate catalyst with a ratio of acid and basic salts, equal to 2.88. Maximum yields of methyl vinyl ketone, obtained under optimum conditions with the above-mentioned catalysts, are not inferior to results obtained, according to literature data, on hydration of vinylacetylene in the liquid phase with mercury catalysts. Investigation of the duration of one contact cycle showed that after 3 hours of use the activity of the catalysts begins to fall as a result of deposition of polymers and resins on their surfaces. The activity of the catalyst may be restored through regeneration at 400-450° in a current of air mixed with steam. The least fall of activity (degree of conversion of vinylacetylene and productivity with regard to methyl vinyl ketone) is observed for a cadmium-calcium-phosphate catalyst in which the ratio $\frac{CdO + CaO}{P_2O_5} = 2.88$. When the duration of one contact cycle was increased from 3 to 6 hours, the degree of conversion of vinylacetylene was reduced from 36 to 30%, and the productivity with regard to methyl vinyl ketone, from 81 to 65 g/liter of cat.–hr. Approximately the same results are obtained for cadmium tungstate. For the rest of the catalysts, increasing the duration of the contact cycle from 3 to 6 hours causes the productivity with regard to methyl vinyl ketone to fall nearly to half.

EXPERIMENTAL

Catalysts

The cadmium-calcium-phosphate catalyst was prepared through precipitation by ammonium phosphate from a mixture of cadmium nitrate and calcium acetate solutions. The precipitate was freed from soluble salts by washing and dried at 100-110°. The content of CdO and CaO in the catalyst amounted to 10 and 90 mole %, respectively.

Cadmium tungstate. This was prepared according to Leffort [16] by treatment of sodium tungstate solution with cadmium acetate:

$$Na_2WO_4 + Cd(CH_3COO)_2 \rightarrow CdWO_4 + 2NaCOOCH_3.$$

The precipitate was freed from soluble salts by washing and dried at 100-110°.

Tungsten trioxide from Kahlbaum.

Zinc oxide. Commercial zinc oxide, type M-1 (GOST 202-41).

All catalysts were compressed from powder into tablets by means of a laboratory hydraulic press.

Vinylacetylene

Technical vinylacetylene, b.p. +5°, obtained by the dimerization of acetylene, was used for the work. Its content of unsaturated compounds amounted to 99%.

The hydration of vinylacetylene was carried out in a silica tube filled with catalyst and placed in an electric furnace. The temperature of the process was measured with a thermocouple, the hot junction of which lay in the midst of the catalyst layer. The addition of water to a triple bond is an exothermic process. At the beginning of the experiment, after admitting the vinylacetylene-steam mixture to the furnace, a slight temperature rise (10-15°) was usually observed. Owing to this, the catalyst temperature before admitting the mixture to the furnace was set a little below that at which the experiment was conducted. Heat was eliminated in the given case through the heat losses of the furnace. Vinylacetylene from a gasometer (through a rheometer) and water from a buret were fed into the contact tube. The reaction products passed through a condenser, a receiver in which the aqueous condensate was collected, and traps filled with hydroxylamine hydrochloride solution for separation of methyl vinyl ketone vapor from the gas. The uncondensed vinylacetylene was collected in a gasometer over saturated sodium chloride solution. The recovery of vinylacetylene in the exhaust gas was determined through absorption by oleum in an Orsat apparatus.

The liquid reaction products consisted of two layers—water and oil; they were analyzed for their methyl vinyl ketone content by means of hydroxylamine hydrochloride. The results of the experiments on hydration of vinylacetylene are given in the table.

The methyl vinyl ketone was isolated from the water layer by rectification for the purpose of identification.

A fraction, b.p. 79-80°, d^{20}_{20} 0.8532, $n^{20}D$ 1.4110 was isolated; m.p. of semicarbazone, 138-140°.

Found: M 68.5, 68.1. C_4H_6O. Calculated : M 70.

For methyl vinyl ketone [2]: b.p. 79-80°, d^{20}_{20} 0.8520, $n^{20}D$ 1.4110; m.p. of semicarbazone, 139-140°.

No other reaction products could be isolated on investigation of the water layer.

On distillation of the oil layer (obtained from experiments done with cadmium-calcium-phosphate catalyst) a fraction with a b.p. of 65-72° (13 mm), which was a dimer of methyl vinyl ketone (2-acetyl-6-methyl-2,3-dihydropyran), and a fraction, b.p. 106° (9 mm), were obtained.

Fraction, b.p. 65-72° (13 mm).

Found %: C 67.83, 68.14; H 8.49, 8.53. M 136.8. $(C_4H_6O)_2$. Calculated %: C 68.57; H 8.57. M 140.

M.p. of semicarbazone, 174-176°.

For the methyl vinyl ketone dimer [17], b.p. 65° (13 mm): m.p. of semicarbazone, 176°.

A fraction, b.p. 106° (9 mm), $n^{20}D$ 1.5386, was also investigated.

Found M 158.5. $(C_4H_4)_3$. Calculated M 156.

Thus this fraction is apparently a trimer of vinylacetylene. Owing to its small quantity, it was not investigated in more detail.

SUMMARY

1. The process of vapor-phase hydration of vinylacetylene to methyl vinyl ketone with certain solid, mercury-free catalysts has been investigated. It has been shown that cadmium tungstate, cadmium-calcium-phosphate, tungsten trioxide, and zinc oxide may be used as catalysts for this process. Cadmium tungstate and cadmium-calcium-phosphate catalyst have the greatest selectivity with respect to methyl vinyl ketone yield.

2. It has been shown that in the vapor-phase hydration of vinylacetylene, besides methyl vinyl ketone (the main reaction product), the by-products, 2-acetyl-6-methyl-2,3-dihydropyran (in the amount of 3-4%) and a polymer of vinylacetylene (in the amount of 1-1.5%), are also formed.

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Synthetic Rubber

Received March 27, 1957

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*Original Russian pagination. See C.B. Translation.

**In Russian.

ON THE REACTION OF AMMONIA WITH METHYL α-CHLOROACRYLATE

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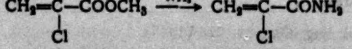
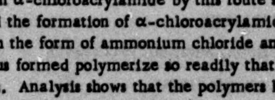
As Klimenko [1] and Beckurts and Otto [2] showed, in the reaction of ammonia with esters of halogen-substituted propionic acids displacement of the alkoxyl radical takes place with formation of the corresponding amides. Klimenko [1] obtained α,α-dichloropropionamide by means of the reaction of dilute ammonia with ethyl α,α-dichloropropionate at room temperature. Beckurts and Otto [2] obtained α-chloropropionamide on shaking ethyl α-chloropropionate with concentrated aqueous ammonia. On the other hand, it is known that in the reaction of ammonia with methyl methacrylate, methacrylamide is obtained in good yield [3].

It was to be expected that the reaction of ammonia with methyl α-chloroacrylate would proceed analogously according to the equation



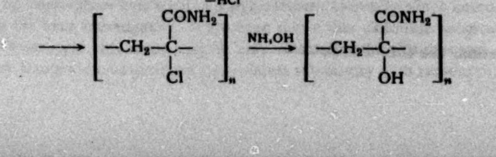
$$CH_2{=}\underset{Cl}{C}{-}COOCH_3 \xrightarrow{NH_3} CH_2{=}\underset{Cl}{C}{-}CONH_2$$

However, the attempt to obtain α-chloroacrylamide by this route showed that an entirely different reaction mechanism prevails here, and the formation of α-chloroacrylamide is not observed. The reaction proceeds with splitting off of chlorine in the form of ammonium chloride and displacement of the alkoxyl radical by the amido group. The amides thus formed polymerize so readily that they could not be isolated from the reaction mixture in monomeric form. Analysis shows that the polymers have the empirical formula $(C_3H_5O_2N)_n$ and apparently are poly-α-hydroxyacrylamides of low molecular weight



$$\left[-CH_2-\overset{OH}{\underset{CONH_2}{C}}-\right]_n, \text{ where } n = 2\text{–}7.$$

Splitting off of chlorine from methyl α-chloroacrylate occurs to the same extent on reaction with either concentrated aqueous or dry, gaseous ammonia at either room temperature or lower ones (from 0 to -25°), whereupon the final polymer isolated from aqueous solutions has the same composition, irrespective of the conditions of the reaction with ammonia. The formation of polymers occurs both in the absence and in the presence of an inhibitor (hydroquinone). Similarly, both with aqueous and with gaseous ammonia under the same conditions (from 0 to -25°), splitting off of chlorine from methyl α, β-dichloropropionate occurs. In both cases, instead of the expected α, β-dichloropropionamide, a polymer of low molecular weight, having the same composition as that obtained in the reaction of ammonia with methyl α-chloroacrylate, $(C_3H_5O_2N)_n$, is isolated as the final product. The mechanism of the reaction of ammonia with methyl α-chloroacrylate and methyl α, β-dichloropropionate may be represented by the scheme



$$CH_2Cl{-}CHCl{-}COOCH_3 \xrightarrow[-HCl]{NH_3} CH_2{=}CCl{-}COOCH_3 \xrightarrow{NH_3}$$

$$\longrightarrow \left[-CH_2-\overset{CONH_2}{\underset{Cl}{C}}-\right]_n \xrightarrow{NH_4OH} \left[-CH_2-\overset{CONH_2}{\underset{OH}{C}}-\right]_n$$

The reaction of splitting off of chlorine from esters of α-chloroacrylic and α, β-dichloropropionic acids have not been described in the literature up to now. Apparently it is a general reaction, characteristic of esters of saturated aliphatic acids containing chlorine in the α, β-position.

EXPERIMENTAL

Methyl α-chloroacrylate was prepared according to Marvel [4] by dehydrochlorination of methyl α, β-dichloropropionate in the presence of freshly distilled quinoline. The reaction mixture was heated to boiling, and methyl α-chloroacrylate was distilled off at 57-59° (55 mm). After distillation through a column containing metallic (copper) packing the methyl α-chloroacrylate had a b.p. of 58° (55 mm), d^{20}_4 1.1892, $n^{20}D$ 1.4400.

Methyl α, β-dichloropropionate was prepared by chlorination of methyl acrylate [5,6].

a) Reaction of aqueous ammonia with methyl α-chloroacrylate at room temperature. To 120.5 g of methyl α-chloroacrylate in a liter flask was added 1.2 g of hydroquinone and 300 ml of aqueous ammonia. The mixture was periodically shaken at room temperature until it became homogeneous. (With vigorous shaking, the reaction continued for 1–1.5 hours with negligible heating). The solution was concentrated in vacuo, and a brown, resinous mass was formed; on fractional crystallization of an aqueous solution of this mass crystals were isolated, which decomposed, without melting, at a temperature over 300°. The crystals gave a reaction for chlorine with $AgNO_3$ and evolved gaseous ammonia on heating with alkali.

Found %: N 26.81; Cl 65.80. M 56. NH_4Cl. Calculated %: N 26.1; Cl 66.3. M 53.5.

Removal of the ammonium chloride was accomplished by careful, gradual solution of the viscous, resinous reaction mass in minimum quantities of water, followed by precipitation with a 5-fold quantity of methyl alcohol. Thereupon the ammonium chloride passed into the water-methanol mixture, and the resin was precipitated, gradually being freed from ammonium chloride. The operation was carried out until there was no reaction for chlorine (with $AgNO_3$). In all, 52.9 g of ammonium chloride (98.9%, calculated on the basis of the original methyl α-chloroacrylate) was removed.

After drying to constant weight in vacuo at room temperature a yellowish-brown polymer (85.2 g, 97.9%) was obtained, which formed a colored, transparent film on evaporation of the solvent. The polymer was readily soluble in water, less so in alcohol, and quite insoluble in other organic solvents (benzene, ether, acetone, dioxan). Softening point in a capillary, 71°.

Found %: C 41.95; H 5.97; N 16.40; OH 96.9 (after Verley). M 600 (cryoscop.). $(C_3H_5O_2N)_7$. Calculated %: C 41.38; H 5.75; N 16.10. n = 7. M 609.

b) Reaction of gaseous ammonia with methyl α-chloroacrylate. For a more detailed study of the mechanism of the reaction of methyl α-chloroacrylate and ammonia, methyl α-chloroacrylate was saturated with gaseous ammonia at a temperature from 0 to -5°. After cooling to 0 to -5°, 82 g of methyl α-chloroacrylate was strongly saturated for 2 hours with ammonia gas from a cylinder, dried with calcium chloride. The flask containing the reaction products was left in solid carbon dioxide overnight. From the reaction mixture, after standing at room temperature, a copious quantity of fine crystals (34.0 g, 92%) of ammonium chloride separated out.

Found %: N 25.63; Cl 66.37. NH_4Cl. Calculated %: N 26.1; Cl 66.3.

After elimination of the ammonium chloride the mother liquor was treated with alcohol, from which were isolated white crystals (4 g), m.p. 122°, which gave a negative reaction for chloride ion.

Found %: C 37.51; H 5.40; N 22.16; Cl 18.61. M (cryoscop.) 181.1. $C_6H_{10}O_2N_3Cl$. Calculated %: C 37.60; H 5.22; N 21.93; Cl 18.53. M 191.5.

The structure of this substance was established.

After elimination of the ammonium chloride and the crystalline substance with a m.p. of 122° the resinous reaction mass was freed from traces of ammonium chloride by the method described above. The remainder of the polymer amounted to 54 g. The polymer was readily soluble in water, less so in alcohol, and quite insoluble in organic solvents (benzene, ether, acetone, dioxan).

Found %: C 41.08; H 5.97; N 16.00. M (cryoscop.) 282.2. $(C_3H_5O_2N)_3$. Calculated %: C 41.38; H 5.75; N 16.10. M 261.

c) Reaction of ammonia with methyl α-chloroacrylate at -20 to -25° in anhydrous chloroform. On the assumption that splitting off of chlorine would occur to a lesser extent under milder conditions, methyl α-chloroacrylate was saturated with ammonia in anhydrous chloroform solution at a temperature from -20 to -25°. Into the reaction mixture, which consisted of 30.0 g of methyl α-chloroacrylate and 15 ml of anhydrous chloroform (cooled to -20 to -25° in an acetone-dry ice mixture), ammonia gas from a cylinder, dried with calcium chloride, was passed for 3 hours. A white, crystalline precipitate (12.3 g) of ammonium chloride separated out from the reaction mixture at room temperature. The resinous reaction mixture was repeatedly dissolved in water and precipitated with acetone until all traces of ammonium chloride were eliminated (reaction with $AgNO_3$). Eighteen and seven-tenths g of the polymer was isolated.

Found %: C 40.95; H 6.05; N 16.38. M (cryoscop.) 182. Hydroxyl groups (after Verley) 99.6%. $(C_3H_5O_2N)_2$. Calculated %: C 41.13; H 5.75; N 16.10. M 174.

d) Reaction of ammonia with methyl-α, β-dichloropropionate. It was of interest to establish the character of the reaction of ammonia with methyl α,β-dichloropropionate. Dry ammonia gas from a cylinder was rapidly passed for 2 hours into a flask containing 100 g of methyl α, β-dichloropropionate at a temperature from 0 to -5°. At room temperature 58.0 g of crystals separated out, and sublimed, without melting, at a temperature over 300°.

Found %: N 26.24; Cl 65.98. NH_4Cl. Calculated %: N 26.10; Cl 66.30.

The resinous reaction mass was repeatedly dissolved in the minimum quantities of distilled water and precipitated with acetone until all traces of ammonium chloride were eliminated. Fifty-two g of a polymer, having a softening point in a capillary, of 102°, and the same properties with respect to solubility as the polymers described above, was isolated.

Found %: C 41.07; N 16.09; H 5.83. M (cryoscop.) 169.5. Hydroxyl groups (after Verley) 98.6%. $(C_3H_5O_2N)_2$. Calculated %: C 41.38; N 16.10; H 5.75. M 174.

SUMMARY

1. It has been established that on treatment of methyl α-chloroacrylate with aqueous ammonia, both at room temperature and at lower temperatures (to 0°), splitting off of chlorine occurs with formation of ammonium chloride and a polymer of low molecular weight. Splitting off of chlorine also occurs in the reaction of methyl α-chloroacrylate with ammonia gas at these and lower temperatures, even if the reaction takes place in a dry chloroform medium.

2. It has been shown that splitting off of chlorine also occurs when aqueous and gaseous ammonia react with methyl α, β-dichloropropionate to form the same final products.

3. A mechanism is suggested for the reactions of methyl α-chloroacrylate and methyl α, β-dichloropropionate with ammonia.

4. It has been shown that the polymer formed is a poly-α-hydroxyacrylamide of low molecular weight.

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Received April 9, 1957

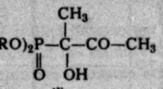
REACTION OF DIALKYL PHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

ESTERS OF 1-HYDROXY-1-ACETOETHYLPHOSPHONIC AND 2-HYDROXY-4-KETO-2-AMYLPHOSPHONIC ACIDS

V. S. Abramov, L. Sh. Belokon' and F. I. Makhmutova

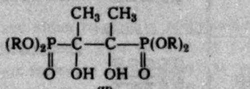
Expanding our previous studies in this field [1], we made a systematic investigation of the condensation of dialkyl phosphorous acids with biacetyl and acetylacetone. The formation of two products—either with one or with two carbonyl groups—could be expected in the condensation of dialkyl phosphorous acids with diketones.

In α-diketones (biacetyl) the carbonyl groups, exerting a mutual influence on each other, enhance polarization. This circumstance should facilitate the condensation of dialkyl phosphorous acids with the first carbonyl group in biacetyl with the formation of substance (I). The reaction of the second carbonyl group with a second molecule of the dialkyl phosphorous acid should depend on the influence exerted by the phosphono group, found in the molecule, on the reactivity of the molecule and the spatial possibilities arising in this connection. Substance (II) should be formed in the case of successful reaction.



$(RO)_2\underset{\underset{O}{\|}}{P}-\overset{\overset{CH_3}{|}}{\underset{\underset{OH}{|}}{C}}-CO-CH_3$

(I)



$(RO)_2\underset{\underset{O}{\|}}{P}-\overset{\overset{CH_3}{|}}{\underset{\underset{OH}{|}}{C}}-\overset{\overset{CH_3}{|}}{\underset{\underset{OH}{|}}{C}}-\underset{\underset{O}{\|}}{P}(OR)_2$

(II)

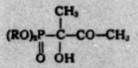
Our investigation revealed that the condensation of dialkyl phosphorous acids with an equimolar amount of biacetyl proceeds well, without a catalyst, if the reaction mixture is heated on the water bath, and is complete in 10–12 hours. The constants of the crude products obtained here are very close to the constants of the vacuum-distilled products. The obtained esters can be vacuum-distilled without decomposition and have a constant boiling point, in contrast to the condensation products of dialkyl phosphorous acids with monoaldehydes and ketones [2]. The stability of the obtained products (I) to heat can be explained by the possible formation of hydroxyl groups as the result of hydrogen bonding with both the oxygen of the phosphono group and the oxygen of the carbonyl group. Evidently, hydrogen bonding with the oxygen of the carbonyl group predominates and makes the phosphorus–carbon bond stable, and consequently the molecule as a whole stable.

The synthesized esters of 1-hydroxy-1-acetoethylphosphonic acid are listed in Table 1.

The esters of 1-hydroxy-1-acetoethylphosphonic acid are colorless sirupy liquids, practically without odor.

The experiments on the condensation of 2 moles of dialkyl phosphorous acids with 1 mole of biacetyl proved unsuccessful. When the reaction products were subjected to fractional distillation we isolated the unreacted dialkyl phosphorous acid (about 50% of that taken), the corresponding ester of 1-hydroxy-1-acetoethylphosphonic acid (67–78%), and a small amount of residue, from which it proved impossible to isolate any definite compound.

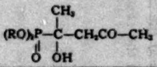
TABLE 1

Esters of 1-Hydroxy-1-acetoethylphosphonic Acid 

$(RO)_2P(=O)-C(CH_3)(OH)-CO-CH_3$

Experiment No.	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Yield (in %)	P (in %)	
					found	calculated		found	calculated
1	CH_3	116° (4mm)	1.4530	1.2391	42.71	42.31	51.0	15.80, 15.93	15.81
2	C_2H_5	120 (4)	1.4450	1.1403	51.05	51.55	55.0	13.76, 13.73	13.84
3	iso-C_3H_7	115 (3)	1.4410	1.1211	60.32	60.78	86.5	12.36, 12.49	12.30
4	C_4H_9	142 (4)	1.4480	1.0641	70.52	70.02	84.0	11.22, 11.11	11.07
5	iso-C_4H_9	131 (3)	1.4430	1.0513	70.63	70.02	86.0	10.91, 11.29	11.07

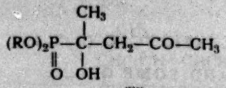
TABLE 2

Esters of 2-Hydroxy-4-keto-2-amylphosphonic Acid 

$(RO)_2P(=O)-C(CH_3)(OH)-CH_2CO-CH_3$

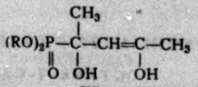
Experiment No.	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D			Unsaturation (%)	Yield (in %)	P (in %)	
					found	calculated				found	calculated
						(IV)	(III)				
1	CH_3	107—108° (3mm)	1.4550	1.1677	48.78	48.14	47.08	40.2	8	14.87, 14.82	14.76
2	C_2H_5	114—115 (3)	1.4450	1.1019	57.48	57.38	56.33	34.0	27	13.25, 13.12	13.02
3	iso-C_3H_7	115—116 (2)	1.4400	1.0542	66.50	66.61	65.56	35.6	14	11.53, 11.82	11.65
4	C_4H_9	139—140 (3)	1.4490	1.0278	77.10	75.80	74.80	30.0	18	10.68, 10.72	10.54
5	iso-C_4H_9	137—138 (4)	1.4470	1.0153	77.30	75.80	74.80	40.0	21	10.97, 10.77	10.54

The condensation of dialkyl phosphorous acids with acetylacetone should proceed with the formation of esters of 2-amylphosphonic acid derivatives. The condensation of a dialkyl phosphorous acid with one carbonyl group of acetylacetone in its carbonyl form yields the ester of 2-hydroxy-4-keto-2-amylphosphonic acid with structure (III), while reaction with the enol form of acetylacetone yields the ester of 2,4-dihydroxy-2-penten-3-yl-phosphonic acid with structure (IV).



$(RO)_2\underset{\underset{O}{\|}}{P}-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2-CO-CH_3$

(III)



$(RO)_2\underset{\underset{O}{\|}}{P}-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH=\underset{\underset{OH}{|}}{C}-CH_3$

(IV)

It is also possible for dialkyl phosphorous acids to add to the double bond of the enolic form of acetylacetone, but then substance (III) should be obtained. In both cases reaction leads to the same product, having two tautomeric forms that are found in equilibrium.

The condensation of dialkyl phosphorous acids with an equimolar amount of acetylacetone proceeds, in the absence of a catalyst, with somewhat more difficulty than in the case of biacetyl. Here fractional distillation of the reaction products gave the corresponding esters in low yields, shown in Table 2.

Two values are given in Table 2 for the calculated molecular refraction: (IV)—for the enolic form, and (III)—for the ketonic form. When the found molecular refractions are compared with the calculated, we find that they lie closer to (IV). The unsaturation of the obtained esters, determined by titration with bromate-bromide solution, permits concluding that the esters of 2-hydroxy-4-keto-2-amylphosphonic acid are enolized to the extent of 30—40%.

An attempt to determine the amount of carbonyl group using phenylhydrazine proved unsuccessful.

The condensation of 2 moles of dialkyl phosphorous acid with 1 mole of acetylacetone failed to give a product with two phosphono groups.

EXPERIMENTAL

Equimolar amounts of dialkyl phosphorous acid and either biacetyl or acetylacetone were mixed; the density and the refractive index of the mixture were determined. Then the mixture was heated in ampules on the water bath. The refraction was measured at periodic intervals; the reaction was considered ended when the refraction remained constant. The products were fractionally distilled in vacuo. The results are given in Tables 1 and 2.

SUMMARY

1. It was shown that dialkyl phosphorous acids condense with both biacetyl and acetylacetone. The corresponding esters—the products of the condensation of equimolar amounts of the reactants—were obtained.

2. The esters of 1-hydroxy-1-acetoethylphosphonic acid are relatively stable to heat (distillation), which is explained by hydrogen bonding of the 1-hydroxy group with the oxygen of the carbonyl group.

3. The esters of 2-hydroxy-2-keto-4-amylphosphonic acid showed 30—40% enolization.

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Received March 5, 1957

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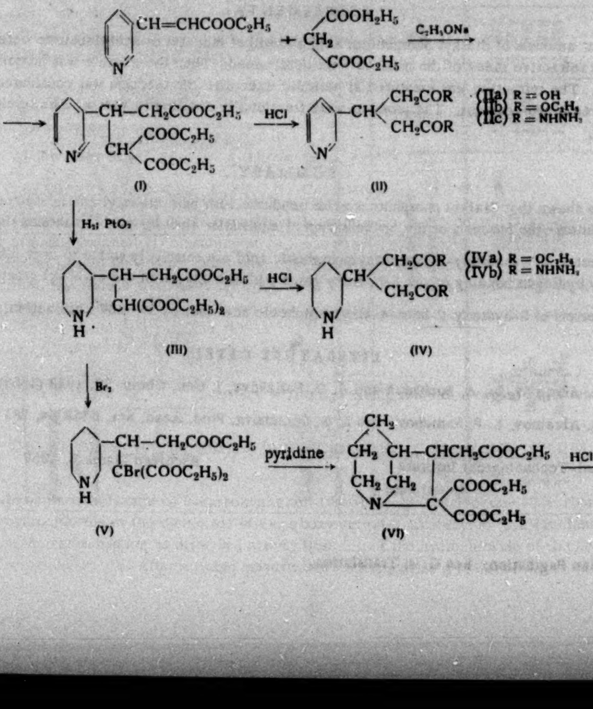
*Original Russian Pagination. See C. B. Translation.

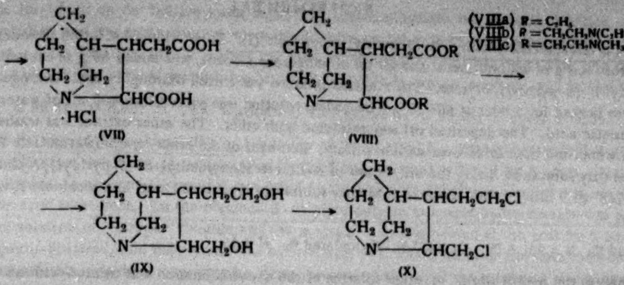
SYNTHESIS OF 6-CARBOXYMETHYL-1-AZABICYCLO (3.2.1) OCTANE-7-CARBOXYLIC ACID AND SOME OF ITS DERIVATIVES

V. Ia. Furshtatova, E. E. Mikhlina and M. V. Rubtsov

A whole series of studies [1–3] has been devoted to the synthesis and biological investigation of quinuclidine (1-azabicyclo (2.2.2) octane) derivatives. At the same time the bicyclic system 1-azabicyclo (3.2.1) octane, isomeric with quinuclidine, has been studied but slightly. Here it is necessary to mention the preparation of only a limited number of 6-monosubstituted 1-azabicyclo (3.2.1) octanes [4]. Disubstituted octanes of the indicated structure were not obtained. In view of the fact that a number of biologically active compounds were found among the 2,3-disubstituted quinuclidine derivatives synthesized by us, it seemed of interest to synthesize the isomeric 6,7-disubstituted 1-azabicyclo (3.2.1) octane derivatives and then compare the biological and chemical properties of the two series of isomeric compounds.

In this paper we describe the synthesis of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid and some of the compounds derived from this acid. The synthesis was accomplished by the following scheme:


CH=CHCOOC₂H₅
COOH₂H₅
CH₂
COOC₂H₅
C₂H₅ONa
CH–CH₂COOC₂H₅
COOC₂H₅
CH
COOC₂H₅
HCl
CH₂COR
CH₂COR
(IIa) R = OH
(IIb) R = OC₂H₅
(IIc) R = NHNH₂
(I)
(II)
H₂; PtO₂
CH–CH₂COOC₂H₅
CH(COOC₂H₅)₂
HCl
CH₂COR
CH₂COR
(IVa) R = OC₂H₅
(IVb) R = NHNH₂
(III)
(IV)
Br₂
CH–CH₂COOC₂H₅
CBr(COOC₂H₅)₂
pyridine
CH₂
CH–CHCH₂COOC₂H₅
COOC₂H₅
COOC₂H₅
HCl
(V)
(VI)


(VII)
(VIII)
(VIIIa) R = C_2H_5
(VIIIb) R = $CH_2CH_2N(C_2H_5)_2$
(VIIIc) R = $CH_2CH_2N(CH_3)_2$
(IX)
(X)

The reaction of the ethyl ester of β-(3-pyridyl) acrylic acid with malonic ester in the presence of an equivalent amount of sodium alcoholate at room temperature or with short heating gave the ethyl ester of β-dicarbethoxymethyl-β-(3-pyridyl)propionic acid (I) in nearly quantitative yield. The boiling of (I) with hydrochloric acid gave β-(3-pyridyl)glutaric acid (IIa), which when heated with an alcohol solution of hydrogen chloride was converted to the diethyl ester (IIb). The dihydrazide (IIc) was obtained from the latter.

In accordance with the indicated scheme, ester (I) was further reduced in the presence of platinum catalyst (of the Adams type) to the ethyl ester of β-dicarbethoxymethyl-β-(3-piperidyl)propionic acid (III). Ester (III), readily soluble in organic solvents and hydrochloric acid, when heated in vacuo (0.1 mm) at 160° is converted to an undistillable solid mass, insoluble in ether, benzene, chloroform and hydrochloric acid. Apparently, here compounds of lactam character are formed under the influence of high temperature. This postulation is supported by the fact that when heated with concentrated hydrochloric acid the solid mass goes into solution. Here the hydrochloride of β-(3-piperidyl)glutaric acid is formed, from which we obtained the corresponding diethyl ester (IVa). The latter was also synthesized by heating ester (III) with hydrochloric acid and subsequent esterification of the resulting diacid. Diester (IVa) was converted to the dihydrazide (IVb).

Ester (III) was also converted to its N-acetyl derivative—the ethyl ester of β-dicarbethoxymethyl-β-(N-acetyl-3-piperidyl)propionic acid.

To synthesize the substituted azabicyclooctane derivatives, ester (III) was treated with bromine in chloroform solution. This gave the ethyl ester of β-dicarbethoxybromomethyl-β-(3-piperidyl) propionic acid (V). The latter when heated with pyridine gave the diethyl ester of 6-carbethoxymethyl-1-azabicyclo (3.2.1)octane-7,7-dicarboxylic acid (VI). Long heating of ester (VI) with hydrochloric acid led to the hydrochloride of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid (VII). Three different methods were used to isolate the free acid: treatment of the hydrochloride of the acid with moist silver oxide and subsequent decomposition of the silver salt of the acid with hydrogen sulfide, treatment of the hydrochloride of the acid with the calculated amount of alcoholic ammonia solution, and long boiling of a water solution of the ethyl ester of 6-carbethoxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid. 6-Carboxymethyl-1-azabicyclo(3.2.1)-octane-7-carboxylic acid exists in two forms—the anhydrous form with m.p. 237°, and the crystallohydrate with m.p. 82°. The latter when heated in vacuo over phosphorus pentoxide at 60°, and also when boiled in anhydrous alcohol, loses water and is transformed to the anhydrous acid with m.p. 237°, which in the air again forms the crystallohydrate.

The heating of hydrochloride (VII) with an alcohol solution of hydrogen chloride gave the diethyl ester of 6-carboxymethyl-1-azabicyclo(3.2.1)octane-7-carboxylic acid (VIIIa). Diester (VIIIa) is also formed by reacting acid (VII) with thionyl chloride, followed by heating the obtained dichloride with alcohol. The reaction of the hydrochloride of the dichloride of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid with diethylaminoethanol and dimethylaminoethanol gave the corresponding esters (VIIIb) and (VIIIc). Diester (VIIIa) was reduced with aluminum lithium hydride to 6-(β-hydroxyethyl)-7-hydroxymethyl-1-azabicyclo (3.2.1)octane (IX). Diol (IX) with thionyl chloride was converted to 6-(β-chloroethyl)-7-chloromethyl-1-azabicyclo (3.2.1)octane (X).

EXPERIMENTAL

Ethyl β-dicarbethoxymethyl-β-(3-pyridyl)propionate (I). To an alcohol solution of sodium ethylate prepared from 5.6 g of sodium metal and 80 ml of anhydrous alcohol, was added 39 g of malonic ester and 43 g of ethyl β-(3-pyridyl)acrylate. The reaction mixture was stirred thoroughly until homogeneous, after which it was heated for 1 hour at 60–63°. The cooled solution was poured into 400 ml of water, containing 15.7 g of acetic acid. The deposited oil was extracted with ether. The ether extract was washed several times with water and then dried over sodium sulfate. Removal of the ether by distillation left 76.5 g (93.5%) of a viscous oily substance, being the ethyl ester of β-dicarbethoxymethyl-β-(3-pyridyl)propionic acid; b.p. 167–168° (0.2 mm). The substance is readily soluble in organic solvents and insoluble in water; $n^{18}D$ 1.4791.

Found %: N 4.15, 4.09. $C_{17}H_{23}O_6N$. Calculated %: N 4.15.

To obtain the hydrochloride an ether solution of the above substance was treated with an alcohol solution of hydrogen chloride until acid to Congo. The deposited oil crystallized on cooling. M.p. 119–120° (from a mixture of alcohol and ether).

Found %: C 54.39, 54.60; H 6.53, 6.26; Cl 9.85, 9.74; N 3.76. $C_{17}H_{23}O_6N \cdot HCl$. Calculated %: C 54.60; H 6.42; Cl 9.46; N 3.75.

β-(3-Pyridyl)glutaric acid (IIa). A mixture of 7 g of ethyl β-dicarbethoxymethyl-β-(3-pyridyl)propionate and 70 ml of concentrated hydrochloric acid was refluxed for 10 hours. The hydrochloric acid solution was concentrated in vacuo, and the residue was dried by treating with anhydrous alcohol three times with removal of the alcohol by distillation between additions. We obtained 4.6 g (100%) of the hydrochloride of the indicated acid. The compound was obtained as colorless crystals, readily soluble in water, difficultly soluble in hot alcohol, and insoluble in cold alcohol, acetone and ether. It was recrystallized from alcohol; m.p. 134.5–135.5° (decompn.).

Found %: C 48.62; H 5.47; N 5.41; Cl 14.45. $C_{10}H_{11}O_4N \cdot HCl$. Calculated %: C 48.88; H 4.88; N 5.7; Cl 14.47.

Ethyl β-(3-pyridyl)glutarate (IIb). A mixture of 4.6 g of β-(3-pyridyl)glutaric acid hydrochloride and 70 ml of a 5% alcohol solution of hydrogen chloride was refluxed for 4 hours. The alcohol was removed in vacuo, and the residue was treated with 50% potash solution and extracted with ether. The ether solution was dried over potash. After removal of the solvent the residue was vacuum-distilled. B.p. 147–149° (0.25 mm). Colorless viscous liquid, soluble in organic solvents and insoluble in water.

Found %: C 62.97, 63.08; H 7.02, 7.09; N 5.48, 5.24. $C_{14}H_{19}O_4N$. Calculated %: C 63.40; H 7.17; N 5.28.

β-(3-Pyridyl)glutaric acid dihydrazide (IIc). A solution of 0.6 g of ethyl β-(3-pyridyl)glutarate and 0.6 ml of hydrazine hydrate in 5 ml of alcohol was heated at the boil for 4 hours. The cooled solution deposited a precipitate, which was filtered and washed with ether. Yield 0.51 g (95.5%). The dihydrazide was obtained as colorless crystals, readily soluble in water and alcohol, and insoluble in ether. M.p. 149–150° (decompn.).

Found %: C 50.29; H 5.95; N 29.42, 29.21. $C_{10}H_{15}O_2N_5$. Calculated %: C 50.63; H 6.33; N 29.52.

Ethyl β-dicarbethoxymethyl-β-(3-piperidyl)propionate (III). A solution of 40 g of ethyl β-dicarbethoxymethyl-β-(3-pyridyl)propionate hydrochloride in 300 ml of anhydrous alcohol was hydrogenated in the presence of 1 g of platinum oxide at room temperature. When the theoretical amount of hydrogen had been absorbed the catalyst was filtered and the filtrate was evaporated in vacuo. The residue resembled caramel. The yield of the hydrochloride of (III) was quantitative. The free base (III), isolated by treating the hydrochloride with 50% potash solution, when heated in vacuo (0.1 mm, 160–200°) was converted to an undistillable solid mass, insoluble in ether, benzene and chloroform. This mass is apparently a lactam type of compound, since it dissolves in hydrochloric acid only when heated.

To characterize the reduction product we synthesized the ethyl ester of β-dicarbethoxymethyl-β-(N--acetyl-3-piperidyl)propionic acid. To obtain this compound we heated the free base (III) with 5 parts of acetic anhydride for 1 hour on the boiling water bath. The acetic anhydride was vacuum-distilled, the residue was dissolved in ether, and the ether solution was washed with aqueous sodium bicarbonate solution and then dried over potash. After distilling off the solvent the residue was vacuum-distilled. B.p. 215° (0.5 mm). The compound is an exceedingly viscous greenish liquid, readily soluble in organic solvents, and insoluble in water.

Found %: C 59.38; H 8.29; N 3.93. $C_{19}H_{31}O_7N$. Calculated %: C 59.22; H 8.05; N 3.64.

Diethyl β-(3-piperidyl)glutarate (IVa). A mixture of 2 g of ethyl β-dicarbethoxymethyl-β-(3-piperidyl)-propionate hydrochloride and 20 ml of concentrated hydrochloric acid was refluxed for 5 hours. Then the solution was evaporated in vacuo, and the residue was dried by treating with anhydrous alcohol 3 times and removing the alcohol after each treatment. To the obtained β-(3-piperidyl)glutaric acid hydrochloride was added 20 ml of an 11% alcohol solution of hydrogen chloride and the reaction mass was heated at the boil for 2 hours. The alcohol was vacuum-distilled, and the residue was treated with 50% potash solution and then extracted with ether. The ether solution was dried over potash. After removal of the ether the substance was vacuum-distilled. B.p. 133–134° (0.4 mm). Yield 1.2 g (87.5%). The diester is a colorless mobile liquid, readily soluble in water and organic solvents; $n^{17}D$ 1.4718.

Found %: C 61.57, 61.60; H 9.08, 9.32; N 5.14. $C_{14}H_{25}O_4N$. Calculated %: C 61.99; H 9.22; N 5.20.

β-(3-Piperidyl)glutaric acid dihydrazide (IVb). A solution of 0.47 g of the diethyl ester of β-(3-piperidyl)-glutaric acid and 0.5 ml of hydrazine hydrate in 5 ml of alcohol was heated at the boil for 4 hours. After distilling off the alcohol and excess hydrazine hydrate the residue crystallized. The crystals were rubbed with ether and filtered. Yield 0.38 g (90.5%). The dihydrazide was obtained as colorless crystals, soluble in water and alcohol, and insoluble in ether. M.p. 148–150° (decompn.).

Found %: C 49.18, 49.27; H 8.63, 8.70. $C_{10}H_{21}O_2N_5$. Calculated %: C 49.32; H 8.64.

Diethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1)octane-7,7-dicarboxylate (VI). Ethyl β-dicarbethoxymethyl-β-(3-piperidyl)propionate hydrochloride, obtained by the reduction of 40 g of the corresponding pyridine derivative, was dissolved in 125 ml of dry chloroform. To the chloroform solution was added in 8 hours a solution of 17.3 g of bromine in 130 ml of dry chloroform at room temperature and with good stirring. The solution decolorized completely in the next 12–14 hours. Then the chloroform was removed in vacuo, the residue was dissolved in 136 ml of water, the aqueous solution was treated with an equal volume of 50% potash solution, and the resulting oil was extracted with ether. The ether solution of the β-dicarbethoxy-bromomethyl-β-(3-pyridyl)propionate (V) was evaporated in vacuo and the remaining oil was boiled for 2 hours with 360 ml of pyridine. Here the reaction mass assumed a dark-brown color. After distilling off the pyridine the remaining dark-brown viscous oil was treated with 50% potash solution and the diethyl ester of 6-carbethoxymethyl-1--azabicyclo (3.2.1)octane-7,7-dicarboxylic acid was extracted with ether. The ether solution was dried over potash, the ether was distilled off, and the residue was vacuum-distilled. B.p. 126–128° (0.1 mm). Yield 29.35 g (80.3%). Colorless mobile liquid, readily soluble in water and organic solvents.

$n^{18}D$ 1.4777, d^{18}_4 1.130, MR_D 85.37; calculated 85.20.

Found %: N 4.19. $C_{17}H_{27}O_6N$. Calculated %: N 4.11.

6-Carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid hydrochloride (VII). A mixture of 15.3 g of diethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1)octane-7,7-dicarboxylate and 150 ml of concentrated hydrochloric acid was heated under reflux for 20 hours. Then the hydrochloric acid solution was decolorized with charcoal and evaporated on the water bath to incipient crystallization. Cooling gave the hydrochloride of 6-carboxymethyl-1-azabicyclo(3.2.1)octane-7-carboxylic acid as lustrous white plates, which were filtered and washed well with acetone. Yield 10.2 g (92.5%). White crystalline powder, readily soluble in water, difficultly soluble in hot alcohol, and insoluble in cold alcohol, acetone and ether. M.p. 232–235° (decompn.).

Found %: C 48.02, 47.77; H 6.28, 6.44; Cl 13.91, 13.78. $C_{10}H_{16}O_4NCl$. Calculated %: C 48.10; H 6.42; Cl 14.22.

6-Carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid. a) Moist silver oxide, prepared from 1.93 g of silver nitrate, was added to a solution of 0.5 g of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7--carboxylic acid hydrochloride in 7 ml of water, and the resulting suspension was shaken for 16 hours. Then the reaction mass was diluted with 40 ml of water, brought to a boil, filtered, and the precipitate washed 4 times with 10 ml portions of hot water. The filtrate was saturated with hydrogen sulfide, the silver sulfide was filtered, and the colorless aqueous solution of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid was evaporated in vacuo to dryness. We obtained 0.3 g of the acid (70.5%) as colorless crystals, readily soluble in water, difficultly soluble in alcohol, and insoluble in ether and benzene. M.p. 237° (decompn.).

b) A solution of 0.2 g of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid hydrochloride in 8 ml of anhydrous alcohol was prepared by heating at the boil. Then the solution was treated with 1.515 ml of alcoholic ammonia solution, containing 0.01365 g of ammonia, and the whole allowed to stand for 60 hours. Colorless crystals of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid deposited during this time. Yield 0.1 g (62.6%). M.p. 237° (decompn.).

Found %: C 55.82, 55.76; H 7.31, 7.00. $C_{10}H_{15}O_4N$. Calculated %: C 56.34; H 7.04.

In air 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid is converted to the crystallohydrate, containing 1/2 H_2O, with m.p. 82°.

Found %: C 53.92, 53.66; H 7.61, 7.54. $C_{10}H_{15}O_4N \cdot 1/2H_2O$. Calculated %: C 54.00; H 7.26.

The crystallohydrate can again be converted to the anhydrous acid with m.p. 237° by drying in vacuo (15 mm) over phosphorous pentoxide at 60°, and also by boiling with anhydrous alcohol.

c) A solution of 2 g of ethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylate in 20 ml of water was heated at the boil for 40 hours. Evaporation of the aqueous solution in vacuo gave 1.4 g of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid as the crystallohydrate. M.p. 82°.

Ethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylate (VIIIa). a) A mixture of 10 g of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid hydrochloride and 100 ml of thionyl chloride was heated on the water bath at 60–65° for 4 hours. The excess thionyl chloride was removed in vacuo. Its complete removal was achieved by adding anhydrous benzene twice with removal of the benzene by vacuum-distillation each time. To the obtained hydrochloride of the acid dichloride was added 100 ml of anhydrous alcohol. The alcohol solution was heated at the boil for 3 hours. The alcohol was vacuum-distilled, the residue was treated with 50% potash solution, and the obtained oil was extracted with ether. The ether solution was dried over potash. The ether was distilled off and the substance was vacuum-distilled. We obtained 9.9 g (91%) of ethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylate with b.p. 130–131° (0.35 mm). The compound is a yellowish oil, readily soluble in organic solvents and in water (with opalescence); $n^{18}D$ 1.4774.

b) A mixture of 10 g of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid hydrochloride and 100 ml of an 11% alcohol solution of hydrogen chloride was heated at the boil for 8 hours. Treatment in the same manner as described in (a) gave 9.2 g (85.3%) of the diester. B.p. 130–131° (0.35 mm), $n^{18}D$ 1.4774.

Found %: C 62.29; H 8.37; N 4.95. $C_{14}H_{23}O_4N$. Calculated %: C 62.45; H 8.55; N 5.21.

Di-(diethylaminoethyl) ester of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid (VIIIb). A mixture of 2 g of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid hydrochloride and 20 ml of thionyl chloride was heated for 8 hours at 60–65°. On conclusion of reaction the excess thionyl chloride was vacuum-distilled, the residue was treated with 20 ml of diethylaminoethanol, and the mixture was heated for 3 hours at 85–90°. The unreacted diethylaminoethanol was distilled off, the obtained ester hydrochloride was treated with 50% potash solution, and the resulting oil was extracted with ether. After drying the ether solution over potash the solvent was distilled off and the residue was vacuum-distilled. We obtained 2 g (60.8%) of the di-(diethylaminoethyl) ester of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid with b.p. 186–188° (0.1 mm). The compound is an oil, readily soluble in organic solvents and in water; $n^{17.3}D$ 1.4855.

Found %: C 63.87, 64.15; H 9.88, 9.93; N 10.26. $C_{22}H_{41}O_4N_3$. Calculated %: C 64.23; H 9.98; N 10.22.

Di-(dimethylaminoethyl) ester of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid (VIIIc). To the hydrochloride of the dichloride of 6-carboxymethyl-1-azabicyclo (3.2.1) octane-7-carboxylic acid, obtained, in the same manner as described above, from 2 g of the hydrochloride of the acid, was added 20 ml of dimethylaminoethanol. After suitable treatment we obtained 1.8 g (63%) of the di-(dimethylaminoethyl) ester of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid as a yellow viscous oil, readily soluble in organic solvents and in water. B.p. 178–180° (0.1 mm); $n^{17.5}D$ 1.4855.

Found %: N 11.77, 11.53. $C_{18}H_{33}O_4N_3$. Calculated %: N 11.83.

6-(β-Hydroxyethyl)-7-hydroxymethyl-1-azabicyclo (3.2.1)octane (IX). A solution of 2 g of ethyl 6-carbethoxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylate in 25 ml of absolute ether was added with stirring to 1 g of aluminum lithium hydride in 25 ml of absolute ether. The reaction mass was heated at the boil for 1 hour. Then 1.85 ml of water was added with good cooling and stirring, and the obtained precipitate of aluminum and lithium hydroxides was filtered and washed well on the filter with chloroform. The ether and chloroform extracts were combined and dried over potash. Removal of the solvents by vacuum-distillation gave 1.3 g (95%) of 6-(β-hydroxyethyl)-7-hydroxymethyl-1-azabicyclo (3.2.1)octane. Colorless viscous oil, readily soluble in water and in chloroform, and more difficultly soluble in ether. B.p. 154° (0.4 mm).

Found %: C 64.75, 64.54; H 9.88, 10.00; N 7.51, 7.16. $C_{10}H_{19}O_2N$. Calculated %: C 64.86; H 10.26; N 7.56.

6-(β-Chloroethyl)-7-chloromethyl-1-azabicyclo (3.2.1)octane (X). To the hydrochloride of 6-(β-hydroxyethyl)-7-hydroxymethyl-1-azabicyclo (3.2.1)octane, obtained from 3.5 g of the free base, was added 30 ml of dry chloroform, followed by the gradual addition of 28 ml of thionyl chloride with cooling. The solution was heated at the boil for 1 hour. The chloroform and excess thionyl chloride were removed in vacuo. The residue was treated with 50% potash solution and the 6-(β-chloroethyl)-7-chloromethyl-1-azabicyclo (3.2.1)octane was extracted with chloroform. The chloroform solution was dried over potash. After removal of the chloroform the dichloro compound was vacuum-distilled. Yield 3.3 g (77.5%). B.p. 105–106° (0.15 mm). The dichloro compound is a colorless mobile liquid, readily soluble in water and organic solvents. On long standing the liquid gradually becomes turbid, apparently due to the formation of a polymer with the properties of a quaternary salt.

Found %: C 54.35; H 7.66. $C_{10}H_{17}NCl_2$. Calculated %: C 54.05; H 7.66.

SUMMARY

Starting with the ethyl ester of β-(3-pyridyl)acrylic acid, the synthesis of 6-carboxymethyl-1-azabicyclo-(3.2.1)octane-7-carboxylic acid was accomplished via the following route: ethyl ester of β-dicarbethoxymethyl-β-(3-pyridyl)propionic acid to the ethyl ester of β-dicarbethoxymethyl-β-(3-piperidyl)propionic acid to the ethyl ester of β-dicarbethoxybromomethyl-β-(3-piperidyl)propionic acid to the diethyl ester of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7,7-dicarboxylic acid.

Together with the indicated compounds, we prepared the diethyl ester of 6-carboxymethyl-1-azabicyclo-(3.2.1)octane-7-carboxylic acid, di-(diethylaminoethyl) and di-(dimethylaminoethyl) esters of 6-carboxymethyl-1-azabicyclo (3.2.1)octane-7-carboxylic acid, 6-(β-hydroxyethyl)-7-hydroxymethyl-1-azabicyclo-(3.2.1)octane and 6-(β-chloroethyl)-7-chloromethyl-1-azabicyclo (3.2.1)octane.

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Received March 16, 1957

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF γ-AMINO KETONES

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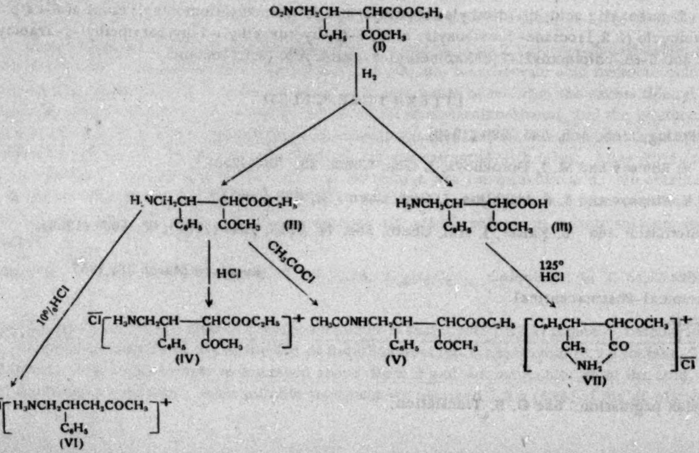
The successful reaction of nitroolefins with acetoacetic ester [1–3] made it possible to use this reaction for developing a new method of obtaining γ-amino ketones, compounds that have been left practically unstudied due to lack of accessible methods for their synthesis, and possessing interest due to the possibility of their heterocyclization to various types of pyrroline derivatives.

It also seemed of interest to establish the relationship between the structure of unsaturated nitro compounds and their ability to condense with acetoacetic ester.

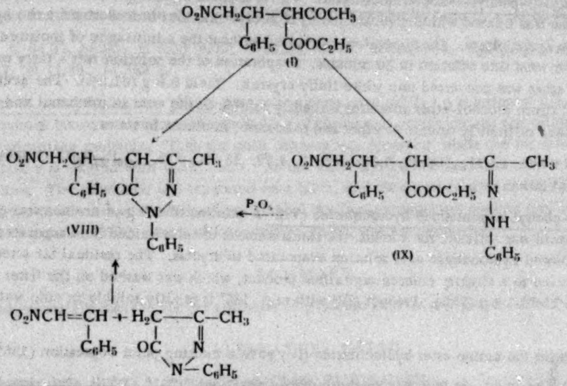
The reaction of nitrostyrene with acetoacetic ester, catalyzed by either triethylamine or pyridine, led to the formation of the ethyl ester of 2-acetyl-3-phenyl-4-nitrobutyric acid (I) in high yields (98 and 82%, respectively). Depending on the length of reaction, the catalytic reduction of the ester gave two products: when the hydrogenation was for 10 hours only the nitro group was attacked and the reduction product was the ethyl ester of 2-acetyl-3-phenyl-4-aminobutyric acid (II), while hydrogenation for 48 hours was accompanied by saponification of the ester and the formation of 2-acetyl-3-phenyl-4-aminobutyric acid (III).

The amino keto ester (II) was subjected to various chemical transformations: 1) saturation of a benzene solution of the ester with dry hydrogen chloride gave the corresponding hydrochloride (IV); 2) treatment of the ester with acetyl chloride gave the acetyl derivative (V); 3) heating the ester with 10% hydrochloric acid led to achieving the main objective: as the result of ketonic cleavage the γ-amino ketone, 1-amino-2-phenyl-4-pentanone (VI), isolated as the hydrochloride, was obtained in 45% yield.

When heated above its melting point the amino acid (III) readily underwent heterocyclization to the pyrrolidone derivative, which when treated with dry hydrogen chloride gave the hydrochloride of 3-phenyl-4-acetyl-5-pyrrolidone (VII).


O₂NCH₂CH—CHCOOC₂H₅ / C₆H₅ COCH₃
(I)
H₂
H₂NCH₂CH—CHCOOC₂H₅ / C₆H₅ COCH₃
(II)
H₂NCH₂CH—CHCOOH / C₆H₅ COCH₃
(III)
10% HCl
HCl
CH₃COCl
125°
HCl
Cl⁻[H₃NCH₂CH—CHCOOC₂H₅ / C₆H₅ COCH₃]⁺
(IV)
CH₃CONHCH₂CH—CHCOOC₂H₅ / C₆H₅ COCH₃
(V)
[C₆H₅CH—CHCOCH₃ / CH₂ CO / NH₂]⁺ Cl⁻
VII)
Cl⁻[H₃NCH₂CHCH₂COCH₃ / C₆H₅]⁺
(VI)

Special attention was given to establishing the structure of condensation product (I). In alcohol medium with phenylhydrazine in the presence of hydrochloric acid it formed the phenylmethylpyrazolone derivative (VIII), which proved to be identical with the reaction product of nitrostyrene and phenylmethylpyrazolone; hydrazone (IX), synthesized from (I), when heated in benzene in the presence of phosphorus pentoxide was converted to pyrazolone (VIII). As a result, the structure of the condensation product of nitrostyrene with acetoacetic ester failed to evoke any doubt.



EXPERIMENTAL

Ethyl 2-acetyl-3-phenyl-4-nitrobutyrate (I). A solution of 0.52 g (0.0035 mole) of ω-nitrostyrene and 0.58 g (0.0045 mole) of ethyl acetoacetate in 5 ml of anhydrous benzene was treated with 4 drops of pyridine. The mixture was kept protected from moisture at 15° for 12 hours. Removal of the solvent by evaporation (at room temperature) gave the ethyl ester of α-acetyl-β-phenyl-γ-nitrobutyric acid [2] as white needle crystals with m.p. 76°. Yield 0.8 g (82%).

Ethyl 2-acetyl-3-phenyl-4-aminobutyrate (II). A suspension of 2 g of freshly prepared skeletal nickel catalyst in 20 ml of methyl alcohol was saturated for 1 hour with hydrogen at room temperature and vigorous shaking until absorption was complete. Then a solution of 2 g of ethyl 2-acetyl-3-phenyl-4-nitrobutyrate (I) in 50 ml of methanol was added in a hydrogen stream, and the hydrogenation run at 18–20° with vigorous shaking for 10 hours; the hydrogen consumed was 480 ml (calculated 481.6 ml). The catalyst was separated by filtration and then washed three times on the filter with 25 ml of methanol. The methanol filtrate was diluted with 3 volumes of cold water. In approximately 30 minutes a white crystalline precipitate deposited from solution, which was dried over alkali. Yield 0.8 g (45%).

Successive recrystallization from ether and then benzene gave the ethyl ester of 2-acetyl-3-phenyl-4-aminobutyric acid as white needles with m.p. 114°; soluble in methanol and ethanol, acetone, benzene, ether, in dilute alkali and mineral acid solutions, and when heated in 10% soda solution; insoluble in water.

Found %: C 67.55, 67.15; H 7.53, 7.42; N 5.95, 5.84. M 267, 221. $C_{14}H_{19}O_3N$. Calculated %: C 67.42; H 7.68; N 5.62. M 249.2.

2-Acetyl-3-phenyl-4-aminobutyric acid (III). To a suspension of 3.2 g of skeletal nickel catalyst, previously saturated with hydrogen, was added a solution of 2 g of (I) in 50 ml of methyl alcohol in a hydrogen stream, and the hydrogenation run at 18-20° with vigorous shaking for 48 hours; the hydrogen consumed was 500 ml (calculated 481.6 ml). Then the reaction mass was worked up in the same manner as in the preceding case. Yield 0.8 g (50.6%). (III) was obtained as white needles with m.p. 125° (from benzene). Its mixture with (II) had m.p. 105°. 2-Acetyl-3-phenyl-4-aminobutyric acid is soluble in methanol and ethanol, acetone, ether, in dilute alkalies, and when heated in 10% soda solution and in mineral acids.

Found %: C 64.92, 64.93; H 7.08, 6.88; N 6.16, 6.06. M 216, 213. $C_{12}H_{15}O_3N$. Calculated %: C 65.12; H 6.83; N 6.33. M 221.1.

Ethyl 2-acetyl-3-phenyl-4-aminobutyrate hydrochloride (IV). Dry hydrogen chloride was bubbled for 10 minutes into a solution of 0.1 g of the amino ester (II) in 10 ml of benzene, and here product (IV) deposited as a white crystalline precipitate with m.p. 171°, exceedingly soluble in water. Yield 0.11 g (99%). Treatment of a water solution of the salt with 10% soda solution resulted in the separation of the original amino ester (II).

Ethyl-2-acetyl-3-phenyl-4-acetamidobutyrate (V). A solution of 1.25 g (0.005 mole) of amino ester (II) in 25 ml of benzene was treated with 3 g (0.042 mole) of acetyl chloride; in a short time the hydrochloride deposited copiously as a precipitate. The suspension was boiled without the admittance of moisture for 4 hours, and here the precipitate went into solution in 30 minutes. Evaporation of the solution left a tarry residue, which when rubbed with ether was converted into white fluffy crystals. Yield 0.9 g (61.5%). The acetyl derivative (V) with m.p. 205° (from alcohol-ether mixture) is readily soluble in the cold in methanol and ethanol, acetone, benzene and dioxan; difficultly soluble in ether and n-hexane; insoluble in water.

Found %: C 66.16, 66.11; H 6.87, 7.12; N 5.13, 4.79. M 290, 312. $C_{16}H_{21}O_4N$. Calculated %: C 65.93; H 7.26; N 4.81. M 291.2.

1-Amino-2-phenyl-4-pentanone hydrochloride (VI). A solution of 0.5 g of amino ester (II) in 25 ml of 10% hydrochloric acid was refluxed for 4 hours, the small amount of tar obtained here separated by filtration, and the slightly colored hydrochloric acid solution evaporated to dryness. The residual tar after rubbing with acetone was converted to a slightly colored crystalline product, which was washed on the filter with small portions of ether. Yield 0.4 g (95%). Product (IV) with m.p. 165° is readily soluble in cold water, methanol and ethanol.

Its mixture with the amino ester hydrochloride (IV) gave a melting point depression (135°).

Found %: N 6.54, 6.33. M 207, 208 (potentiometric titration). $C_{11}H_{16}ONCl$. Calculated %: N 6.55. M 213.6.

3-Phenyl-4-acetyl-5-pyrrolidone hydrochloride (VII). Amino ester (III) (0.2 g) was heated to the melting point (125°) and then kept at this temperature for 5 minutes. The brown tar obtained here was dissolved in 5 ml of benzene and the solution saturated with dry hydrogen chloride until it showed acid. The tar, isolated after evaporation of the benzene, was converted by rubbing with acetone to a colored crystalline product, which was filtered and washed with small portions of ether. Yield 0.10 g (50%). M.p. 168°. The compound is readily soluble in water; its mixture with amino ketone hydrochloride (VI) gives a melting point depression.

1-Phenyl-3-methyl-4-(α-phenyl-β-nitroethyl)-5-pyrazolone (VIII). A hot solution of 1 g (0.0036 mole) of nitro ester (I) in 20 ml of alcohol was treated with 0.4 g (0.0037 mole) of phenylhydrazine and 3 drops of concentrated hydrochloric acid. The mixture was brought to a boil. After standing at room temperature for a week the solution deposited coarse transparent crystals as long rods with m.p. 85° (from ethanol). Yield 0.6 g (69%).

Reaction of ω-nitrostyrene with 1-phenyl-3-methyl-5-pyrazolone. Synthesis of pyrazolone derivative (VIII). a) A solution of the sodio derivative of 1-phenyl-3-methyl-5-pyrazolone (obtained by the addition of 0.5 g of sodium metal to a solution of 1.74 g of phenylmethylpyrazolone in 30 ml of anhydrous methanol) was treated at 10–15° with a solution of 1.49 g of nitrostyrene in 20 ml of anhydrous methanol. The mixture was heated without the admittance of moisture for 2 hours at 50–55°; the red solution after cooling was neutralized with glacial acetic acid, and then was saturated at 0–5° with dry hydrogen chloride until it showed acid. A finely crystalline precipitate deposited when the pale yellow solution was poured into a mixture of ice and soda, which after 2 hours was filtered and washed with cold water. Yield 3 g (92.8%). Product (VIII) was obtained slightly colored, has a finely crystalline structure, and is soluble in methanol and ethanol, acetone, ether, and in dilute alkali and hydrochloric acid solutions (when heated). M.p. 85° (ethanol).

b) A mixture of 1.49 g of nitrostyrene in 20 ml of anhydrous methanol and 1.74 g of phenylmethylpyrazolone in 30 ml of anhydrous methanol was treated with 6 drops of Rodionov catalyst (alcohol solution of trimethylphenylammonium hydroxide). The mixture was kept at 15–20° for 12 hours without the admittance of moisture. Removal of the solvent by evaporation left coarse transparent crystals with m.p. 85° (ethanol).

Its mixture with product (VIII) did not depress the melting point. Yield 3 g (92.8%).

Found %: C 66.79, 67.13; H 5.60, 5.45; N 12.92, 12.76. M 316, 305. $C_{18}H_{17}O_3N_3$. Calculated %: C 66.83; H 5.30; N 13.02. M 323.2.

Ethyl 2-acetyl-3-phenyl-4-nitrobutyrate phenylhydrazone (IX). A hot solution of 1 g (0.0036 mole) of nitro ester (I) in 20 ml of alcohol was treated with 0.4 g (0.0037 mole) of phenylhydrazine. After standing for a week at room temperature the separated tarry substance was pressed on porous plate. Yield 0.8 g (60.6%). Phenylhydrazone (IX) was obtained as white crystals with m.p. 108° (ethanol); readily soluble in benzene, acetone and ether, and less soluble in methanol and ethanol. It gradually turns to a tar on long standing.

Found %: C 64.91, 64.98; H 6.30, 6.02; N 11.33, 11.42. M 364, 383. $C_{20}H_{23}O_4N_3$. Calculated %: C 65.04; H 6.27; N 11.38. M 369.2.

Conversion of phenylhydrazone (IX) to pyrazolone derivative (VIII). A solution of 0.3 g of hydrazone (IX) in 25 ml of anhydrous benzene was treated with 0.10 g of phosphorus pentoxide and the mixture refluxed for 4 hours without admitting moisture. Then the cold benzene was decanted, while the tar remaining on the bottom of the flask was treated with warm water. As the water cooled, the tar when rubbed with a rod gradually became crystalline. The substance was separated on a filter, and then washed with several portions of water. Yield 0.15 g (58%). After recrystallization from alcohol the finely crystalline product had m.p. 85°. Its mixed melting point with product (VIII), obtained from compound (I), was not depressed.

SUMMARY

A new and accessible method for the synthesis of γ-amino ketones was proposed.

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Received January 21, 1957

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF VINYL MONOMERS

III. SYNTHESIS OF COMPOUNDS WITH A CARBONYL GROUP

A. Ia. Iakubovich, V. V. Razumovskii and I. N. Beliaeva

One of the convenient methods for the synthesis of aryl alkenyl ketones, having general significance, is the Mannich reaction.

Statements have been made that in a number of cases the ease with which the Mannich reaction proceeds is dependent on the nature of the free base used. Thus, Levvy and Nisbet [1] state that 2-acetylfuran and formaldehyde react with the salts of dimethylamine and dipropylamine, but do not react with the salt of diethylamine. Mannich and Heilner [2] described the preparation of phenyl vinyl ketone using dimethylamine hydrochloride. Young and Roberts [3] used diethylamine hydrochloride in the preparation of the same ketone. We used both of the indicated salts in the synthesis of phenyl vinyl ketone, and became convinced that the reaction proceeds much slower and the yield of dialkylaminopropiophenone hydrochloride is much lower when diethylamine hydrochloride is used than when dimethylamine hydrochloride is used (63 and 73.5%, respectively). Phenyl isopropenyl ketone was synthesized from dimethylaminomethylpropiophenone, the latter having been prepared by the method described by Knott [4]. It proved that propiophenone and paraformaldehyde do not react with diethylamine hydrochloride.

The Mannich method was also used by us to obtain the previously unknown 2,5-dichlorophenyl vinyl ketone. 2,5-Dichloroacetophenone and paraform react with diethylamine hydrochloride only to a very slight degree. The reaction with dimethylamine hydrochloride proceeds more easily; the obtained dimethylamino-2,5-dichloropropiophenone hydrochloride had m.p. 162°. 2,5-Dichlorophenyl vinyl ketone was obtained as a slightly green liquid with b.p. 106—107° (5 mm). The ketone polymerizes with extreme ease when distilled, even when distilled in vacuo in the presence of inhibitor. In connection with the greater tendency shown by 2,5-dichlorophenyl vinyl ketone to polymerize when compared with the unsubstituted phenyl vinyl ketone, it is interesting to mention that 2,5-dichlorostyrene also polymerizes more easily than does unsubstituted styrene itself [5]. In the literature relating to the simpler unsaturated aldehydes acrolein and methacrolein, only patent data exist on the preparation of the oximes of these aldehydes. The method described for the preparation of acrolein oxime is based on the conventional reaction with hydroxylamine [6]. Methacrolein oxime was obtained from the addition product of nitrosyl chloride to isobutylene [7,8]. We synthesized the latter oxime by reacting methacrolein with hydroxylamine. The reaction proceeds with ease and gives the oxime in 65% yield. In contrast to acrolein oxime, for which polymers are described [9], methacrolein oxime under block polymerization conditions, when either benzoyl peroxide or azobisisobutyronitrile is used as polymerization initiator, does not polymerize.

EXPERIMENTAL

Phenyl vinyl ketone was obtained by the method of [2]. The yield of dimethylaminopropiophenone hydrochloride was 73.5%.

Found %: Cl 16.29. $C_{11}H_{16}ONCl$. Calculated %: Cl 16.64.

When the synthesis was run using diethylamine hydrochloride the diethylaminopropiophenone hydrochloride was obtained crystalline only after the reaction mixture had been evaporated to small volume. In this case the yield of the ketone was 63%.

The pyrolysis of dimethylaminopropiophenone hydrochloride was run in a vacuum (at a pressure of 5 mm). A mixture of 30 g of the hydrochloride and 0.5 g of hydroquinone was heated at 200–210°. The volatile pyrolysis products were collected in the range 70–120°, dried over sodium sulfate, and fractionally distilled several times in vacuo (with the addition of hydroquinone). We obtained 8.3 g (45%) of phenyl vinyl ketone.

B.p. 74–76° (4 mm), d^{20}_4 1.0387, $n^{20}D$ 1.5550.

From [3]: B.p. 72–73° (3 mm).

Phenyl isopropenyl ketone was obtained from dimethylaminomethylpropiophenone hydrochloride, the latter having been prepared by the Knott method [4]. This hydrochloride was pyrolyzed in the same manner as in the preceding synthesis. Yield of phenyl isopropenyl ketone 48.7%, based on the salt of the Mannich base, or 33.6%, based on starting propiophenone.

B.p. 83.5–85° (7 mm), d^{20}_4 1.0139, $n^{20}D$ 1.5373.

Found %: C 82.01; H 5.9. $C_{10}H_{10}O$. Calculated %: C 82.19; H 6.85.

When an attempt was made to react diethylamine with propiophenone and paraformaldehyde the diethylamine hydrochloride was recovered practically unchanged from the reaction mixture. The starting propiophenone was prepared by the Read method [10].

2,5-Dichlorophenyl vinyl ketone. A mixture of 25 g of 2,5-dichloroacetophenone, 4.4 g of paraformaldehyde, 12.6 g of dimethylamine hydrochloride, 50 ml of anhydrous alcohol and 0.2 ml of concentrated hydrochloric acid was heated with stirring for 6 hours on the boiling water bath. Then the mixture was poured into a dish and allowed to stand overnight in a desiccator. The obtained crystals were filtered and washed with dry ether. We obtained 16 g of dimethylamino-2,5-dichloropropiophenone hydrochloride.

After recrystallization from anhydrous alcohol, m.p. 162°.

Found %: Cl 12.59; N 4.77. $C_{11}H_{14}ONCl_3$. Calculated %: Cl 12.55; N 4.95.

The hydrochloride was pyrolyzed in the same manner as in the preceding syntheses. The yield of 2,5-dichlorophenyl vinyl ketone, obtained as a slightly green liquid, was 17.2%, based on starting 2,5-dichloroacetophenone.

B.p. 106–107° (5 mm), d^{20}_4 1.320, $n^{20}D$ 1.5698, MR 49.90; calculated 49.44.

Found %: C 53.85, 54.10; H 2.99, 3.30; Cl 37.43, 37.32. $C_9H_6OCl_2$. Calculated %: C 53.75; H 2.99; Cl 35.36.

When vacuum-distilled the ketone showed substantial polymerization even in the presence of an inhibitor. The starting 2,5-dichloroacetophenone was prepared [11] by heating a mixture of 50 g of p-dichlorobenzene, 50 g of acetyl chloride and 100 g of aluminum chloride on the boiling water bath for 5 hours. At the end of reaction the mixture was poured on ice, 30 ml of concentrated hydrochloric acid was added, and the product was steam-distilled. The distillate was extracted with ether. Fractionation in vacuo gave a fraction with b.p. 109–113° (7 mm). Yield of 2,5-dichloroacetophenone 50%.

Methacrolein oxime. A solution of 11 g of hydroxylamine hydrochloride in 30 ml of water, containing 0.5 g of N-phenyl-β-naphthylamine (antioxidant), was gradually treated with 7.5 g of sodium carbonate. When all of the sodium carbonate had dissolved the mixture was cooled to -10°, and then 10 g of methacrolein was added dropwise to it in 30–40 minutes with stirring. After stirring for another 15 minutes at -10° the obtained organic layer was separated from the bottom water layer. The water layer was extracted twice with ether, and the ether extract was added to the upper layer. The ether solution was then washed with water and dried over calcium chloride. The residue obtained after distilling off the ether was vacuum-distilled in the presence of N-phenyl-β-naphthylamine. After two distillations we obtained 8 g (65%) of methacrolein oxime.

B.p. 48.5° (12 mm), d^{20}_4 0.9487, $n^{20}D$ 1.4852, MR 25.69; calculated 24.21.

Literature data: B.p. 51–53° (15 mm); 45–48° (6 mm); 143–148° (760 mm).

According to [7]: $n^{19.5}D$ 1.4430; [8]: $n^{20}D$ 1.4789.

Found %: C 58.20, 57.98; H 8.46, 8.38; N 16.54, 16.70. C_4H_7ON. Calculated %: C 56.43; H 8.31; N 16.47.

The methacrolein used for the synthesis was prepared by the oxidation of methallyl alcohol, using the method of Church and Lynn [12].

SUMMARY

1. The Mannich method was used to synthesize phenyl vinyl ketone, phenyl isopropenyl ketone and the previously unknown 2,5-dichlorophenyl vinyl ketone. It was established that propiophenone and paraformaldehyde react with dimethylamine hydrochloride in the Mannich sense, but do not react with diethylamine hydrochloride.

2. Methacrolein oxime was synthesized by the reaction of methacrolein with hydroxylamine.

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Received January 24, 1957

SYNTHESIS OF DIUREINES OF SOME NITROPHENANTHRENEQUINONES

D. F. Kutepov, A. A. Potashnik and D. N. Khokhlov

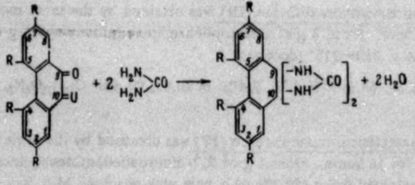
Phenanthrenequinonediureine (I) was obtained by Grimaldi [1] by the fusion of phenanthrenequinone with a large excess of urea at 250°. The author indicates that the isolation and purification of (I) present great difficulties due to the insolubility of both (I) and the other transformation products of urea, found in large amounts in the melt.

It is known that the diureines of α-diketones are easily obtained by reacting urea with the diketone in either aqueous or alcoholic medium in the presence of mineral acid [2,3].

Considering the similarity in the chemical properties of α-diketones and o-quinones, we extended the indicated reaction to phenanthrenequinone and its nitro derivatives. The diureines are formed using an acidulated boiling aliphatic alcohol as the medium. The reaction rate depends on the boiling point of the alcohol. If (I) is formed in small amount under the conditions of prolonged boiling in ethyl alcohol as the medium, then in n-butyl alcohol medium the reaction is ended in 3 hours and the yield of product is 85.5%.

Using similar conditions we obtained the previously unknown diureines in 70.3–88.5% yield: 2-nitrophenanthrenequinonediureine (II), 4-nitrophenanthrenequinonediureine (III), 2,7-dinitrophenanthrenequinonediureine (IV) and 4,5-dinitrophenanthrenequinonediureine (V).

According to the literature [2,3], the diureines of α-diketones are compounds with two imidazole rings; apparently, the diureines (I–V), obtained by us from a quinone and urea by the scheme given below, also contain two imidazole rings in the molecule



where R = H or NO_2.

It was established that the position and number of nitro groups in the phenanthrenequinone molecule exert great influence on the reaction rate of the latter with urea. A nitro group in position 4 and two nitro groups in the 4,5 positions facilitate condensation of the quinone with urea, whereas a nitro group in position 2 and two nitro groups in the 2, 7 positions greatly hinder this reaction when compared with the reaction of unsubstituted phenanthrenequinone with urea.

The reaction rate of the quinones investigated by us with urea decreases in the order: 4-nitrophenanthrenequinone, 4,5-dinitrophenanthrenequinone, unsubstituted phenanthrenequinone, 2-nitrophenanthrenequinone, and 2,7-dinitrophenanthrenequinone. Thus, for example, in boiling ethyl alcohol the reaction for the formation of (III) and (V) is ended in 1.5–2 hours, (I) is formed in small amount after heating for many hours, while (II) and (IV) are not obtained under these conditions. In boiling n-butyl alcohol (b.p. 117°), (III) and (V) are obtained in good yields when the heating is for 1 hour, (I) is obtained in good yield when the heating is for 3 hours, while

(II) and (IV) are formed only in small yields when the heating is for many hours; however, the last two diureines were obtained in good yields when the reaction was run in isoamyl alcohol medium (b.p. 132°).

The alcohol was used in such amount that the quinone went into solution on heating. The reaction can also be run successfully with a smaller amount of the alcohol (here a part of the quinone remains undissolved), but in this case the reaction mixture has to be heated for a much longer time.

To acidulate the medium we used concentrated sulfuric acid in an amount of about 1 ml per 100 ml of solution. Increasing the amount of acid 2–3 times was without appreciable effect on the reaction rate or the yield of diureine. However, a greater acidulation of the medium leads to the formation of tarry substances.

All of the diureines obtained by us are white or slightly colored amorphous powders, insoluble in water and in organic solvents. They do not have melting points, and decompose when heated in a capillary above 300°.

EXPERIMENTAL

Phenanthrenequinonediureine (I). A mixture of 10 g of phenanthrenequinone and 8 g of urea was dissolved in 200 ml of boiling n-butyl alcohol. Then 2 ml of sulfuric acid was added in drops and with stirring to the solution, and the whole boiled under reflux for 3 hours. The deposited (I) was filtered hot, washed with hot ethyl alcohol, then with hot water, and dried. Yield 12.0 g (85.5%). The compound was obtained as a pale orange amorphous substance. M.p. 336–339°.

Found %: C 65.61, 65.25; H 4.52, 4.50; N 18.81, 18.70. $C_{16}H_{12}O_2N_4$. Calculated %: C 65.74; H 4.14; N 19.17.

According to the literature this amorphous powder does not have a melting point. It decomposes when heated strongly, and is insoluble in the common solvents [1].

2-Nitrophenanthrenequinonediureine (II). A mixture of 7.5 g of 2-nitrophenanthrenequinone and 7.5 g of urea was dissolved in 1 liter of isoamyl alcohol (b.p. 132°) with heating, then 10 ml of sulfuric acid was added, and the whole boiled under reflux for 5 hours. (II) was filtered hot, washed with hot glacial acetic acid, then with hot water, and dried. Yield 7.0 g (70.0%); pale yellow powder. M.p. 303–306° (decompn.).

Found %: C 56.44, 56.50; H 3.14, 3.45; N 19.87, 19.66. $C_{16}H_{11}O_4N_5$. Calculated %: C 56.96; H 3.26; N 20.77.

4-Nitrophenanthrenequinonediureine (III) was obtained by the same method used to obtain (I), but here the boiling was for 1 hour. From 5 g of 4-nitrophenanthrenequinone and 5 g of urea we obtained 5.9 g (88.5%) of a white powder. M.p. 310–315° (decompn.).

Found %: C 56.93, 56.60; H 2.70, 2.40; N 20.63, 20.46. $C_{16}H_{11}O_4N_5$. Calculated %: C 56.96; H 3.26; N 20.77.

2,7-Dintrophenanthrenequinonediureine (IV) was obtained by the same method used to obtain (II), but here the heating was for 10 hours. From 1 g of 2,7-dinitrophenanthrenequinone and 1 g of urea in 100 ml of isoamyl alcohol we obtained 0.9 g (70.3%) of a pale pink powder. M.p. 342–345° (decompn.).

Found %: C 50.33, 50.42; H 2.90, 2.94; N 20.77, 20.69. $C_{16}H_{10}O_6N_6$. Calculated %: C 50.26; H 2.64; N 21.99.

4,5-Dinitrophenanthrenequinonediureine (V) was obtained in the same manner as (III). From 2 g of 4,5-dinitrophenanthrenequinone and 2 g of urea in 100 ml of n-butyl alcohol we obtained 2.2 g (86.0%) of a white powder. M.p. 305–308° (decompn.).

Found %: C 51.13, 50.87; H 2.70, 2.65; N 22.12, 21.74. $C_{16}H_{10}O_6N_6$. Calculated %: C 50.26; H 2.64; N 21.99.

SUMMARY

1. A practical and convenient method was developed for the synthesis of the diureines of phenanthrenequinone and its nitro derivatives in 70.3–88.5% yield.

2. The previously unknown 2-nitro-, 4-nitro-, 2,7-dinitro- and 4,5-dinitrophenanthrenequinonediureines were synthesized.

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Received July 8, 1957

CATALYTIC POLYMERIZATION OF POLYPHENYL- AND POLY(DIMETHYLPHENYL)SILOXANES

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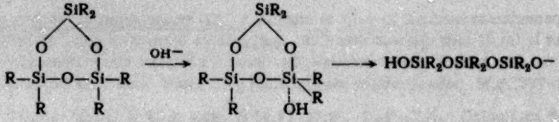
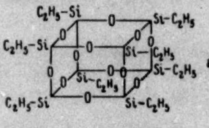
Polyorganosiloxanes are obtained by the hydrolysis of alkyl(aryl)halosilanes or alkyl(aryl)alkoxysilanes with subsequent condensation of the hydrolysis products to polyorganosiloxanes. During hydrolysis, reactions occur that lead to the formation of either linear or cyclic polymers. The cyclic polymers are obtained in the best yield in acid medium, when the hydrolysis is run in an excess of water.

The hydrolysis of bifunctional monomers (dimethyldichlorosilane, phenylmethyldichlorosilane) led to obtaining low-molecular cyclic products—trimers, tetramers and higher cycles [1]. In the presence of catalysts (sulfuric acid, antimony pentachloride [2], potassium hydroxide [3], ferric chloride [4]), the cyclic compounds obtained in the hydrolysis of the bifunctional compounds are capable of rearrangement with rupture of the cycles. Thus, the polymerization of the cycles obtained from dimethyldichlorosilane, under the influence of caustic alkalies, proceeds by the scheme

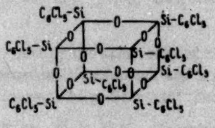

SiR₂
O
O
R—Si—O—Si—R
R
R
OH⁻
SiR₂
O
O
R—Si—O—Si—R
R
R
OH
HOSiR₂OSiR₂OSiR₂O—

Recently it was established that the hydrolysis of trifunctional compounds in acid medium also results in the formation of cyclic polymeric compounds.

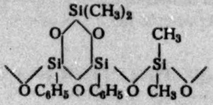
The hydrolysis of ethyltriethoxysilane [5] and pentachlorophenyltrichlorosilane [6] gave crystalline cyclic polymers with the structure


C₂H₅-Si
Si-C₂H₅
C₂H₅-Si
Si-C₂H₅
Si-C₂H₅
Si-C₂H₅
C₂H₅-Si
Si-C₂H₅
O

and


C₆Cl₅-Si
Si-C₆Cl₅
C₆Cl₅-Si
Si-C₆Cl₅
Si-C₆Cl₅
Si-C₆Cl₅
C₆Cl₅-Si
Si-C₆Cl₅
O

The cohydrolysis of phenyltrichlorosilane with dimethyldichlorosilane in acid medium also gives cyclic polymers of a mixed type (A).


Si(CH₃)₂
O
O
CH₃
Si
Si
Si
O C₆H₅ O C₆H₅ O CH₃ O

(A)

Due to the importance of the conversion of tri- and bifunctional alkyl(aryl)halosilanes to polymers, an attempt was made in the present work to study the alkaline catalytic polymerization of the cyclic compounds obtained in the hydrolysis of phenyltrichlorosilane, and also of the cohydrolysis products of phenyltrichlorosilane with dimethyldichlorosilane.

Comparative experiments on the polymerization of octamethylcyclotetrasiloxane and poly(dimethylphenyl)cyclosiloxane with sodium hydroxide revealed that a noticeable change in the viscosity of the product was not observed when octamethylcyclotetrasiloxane was treated with 1% NaOH at 20° for a long time, but that the viscosity rose rapidly when the reaction temperature was raised to 120–130°. However, for the cohydrolysis products of phenyltrichlorosilane with dimethyldichlorosilane (polydimethylphenylcyclosiloxane), treatment with 1% NaOH at 20° causes the viscosity to increase rapidly and the polymer to change to a gel within 35–40 minutes.

To study the influence of the amount of NaOH on the rates of viscosity increase and gel formation at 20° we used a 58% toluene solution of the cohydrolysis products of phenyltrichlorosilane with dimethyldichlorosilane. The experimental data, shown in Fig. 1, reveal that the time required for transition of the polymer into a gel is inversely proportional to the amount of added sodium hydroxide. The relationship between the viscosity and the time of polymerization in the presence of various amounts of catalyst is shown in Fig. 2. The rate of rise in the viscosity of the polymer increases with increase in the amount of catalyst. In addition, the greater the amount of alkali taken, the lower is the viscosity of the polymer at which it changes into a gel. Thus, with 0.9% NaOH the polymer changes into a gel within 30 minutes and a 10% solution of the polymer in toluene has a relative viscosity of 1.5 at the point of transition into a gel, whereas with 0.1% alkali the relative viscosity of the polymer at the transition point is greater than 2.8, and it takes 5.7 hours for the polymer to change to a gel. Curve 6 in Fig. 2 shows the increase in the viscosity of the cyclic polymer obtained from phenyltrichlorosilane when treated with 0.9% sodium hydroxide at 40°. It is interesting to mention that for the given polyphenylsiloxane at 20° and the indicated amount of alkali an increase in the viscosity is not observed even after some 20–30 hours. As can be seen from Fig. 2, for the given polyphenylsiloxane even at 40° the viscosity increases with time more slowly than in the case of the poly(dimethylphenyl)siloxane at 20° and 0.3% sodium hydroxide.

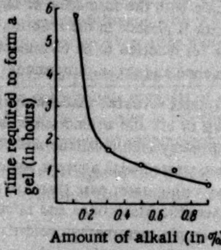


Fig. 1. Effect of amount of alkali on rate of gel formation.

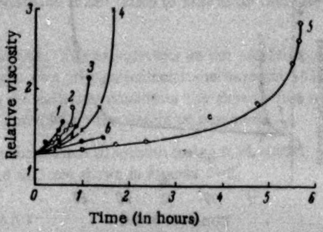
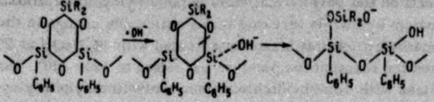


Fig. 2. Relationship between the viscosity and the time of polymerization with various amounts of alkali. Amount of alkali (in %): 1) 0.9, 2) 0.7, 3) 0.5, 4) 0.3, 5) 0.1, 6) 0.9 (40°).

In contrast to octamethylcyclotetrasiloxane, the cyclic polymers obtained by the cohydrolysis of phenyltrichlorosilane with dimethyldichlorosilane, show polymerization at 20° even in the presence of 0.1% NaOH, and the polymers, obtained from phenyltrichlorosilane, in the presence of 0.9% NaOH at 40°.

To determine the influence of concentration on the conversion rates of the poly(dimethylphenyl)siloxanes we ran some experiments with solutions of the polymer in toluene at a concentration of 40, 52.3, 58 and 71%, in the presence of 0.3% NaOH. As can be seen from Fig. 3, the rate of increase in the viscosity decreases and the time required for transition of the polymer into a gel increases as the concentration of the polymer is reduced.

It is possible to assume that the first stage in the reaction with alkali is the formation of an intermediate activated complex due to reaction of the donor hydroxyl group of the sodium hydroxide with the silicon atom.



Such an activated complex causes rupture of the weakened silicon— oxygen bond and forms an ion.

The presence of steric hindrance in the cycle, weakening the strength of the bonds in the molecules, should facilitate progress of this reaction. The formed ion attacks a second cyclic molecule, rupturing the Si–O bond, and adds to it. In this manner, both the molecular chain and its branching increase. The final moment of reaction should be closure of the high-molecular molecule with the formation of larger cycles. If a rupturing factor is present in the reaction sphere then it is possible for reaction to be terminated by the formation of branched and three-dimensional polymers.

The experiments revealed that the cycles, formed in the cohydrolysis of bi- and trifunctional compounds, in particular of dimethyldichlorosilane and phenyltrichlorosilane, when treated with aqueous sodium hydroxide are converted with greater ease than are the cycles obtained from phenyltrichlorosilane and bifunctional monomers, for example, octamethylcyclotrisiloxane. The process for the polymerization of the cyclic products obtained from phenyltrichlorosilane and from phenyltrichlorosilane with dimethyldichlorosilane proceeds with the formation of soluble polymers, and only when a certain viscosity is reached, different for each catalyst concentration used, is a transition of the polymer from a soluble to an insoluble gel-like state observed. The fact that the time required to form a gel is inversely proportional to the amount of added caustic indicates that the more caustic introduced into the reaction, the greater the number of active particles formed per unit of time, and the more rapid is the growth of the molecular chains, and therefore the viscosity.

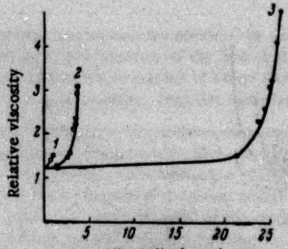


Fig. 3. Effect of the concentration of solutions of the polymer in toluene on the rate of increase in the viscosity.
Concentration of solutions (in %): 1) 71, 2) 52.3, 3) 40.

With reduction in the solution concentration of the polymer the rate of increase in the viscosity decreases and the time required to form a gel increases. This can be explained by stating that the number of cyclic molecules per unit volume of reaction mixture decreases with increase in the dilution, which leads to a reduction in the number of contacts between the cyclic molecules and the growing active centers, as a result of which the reaction rate is lowered.

The greater rate at which the cycles are rebuilt in the case of the poly(dimethylphenyl)siloxanes, when compared to the polyphenylsiloxanes, should be explained as being due to the steric hindrance created by the phenyl groups.

EXPERIMENTAL

Preparation of polyphenylsiloxane. A mixture of 2600 g of water and 634.5 g of toluene was charged into the hydrolyzer, fitted with a water jacket, thermometer and dropping funnel. Then a solution of 634.5 g of phenyltrichlorosilane in 634.5 g of toluene was added to the hydrolyzer with constant stirring. The temperature of the reaction mixture was kept constant at 20°. Then the mixture was stirred for another hour, after which the polymer was separated from the water, washed with water until neutral to Congo, and dried to constant weight. A hard brittle product with m.p. 43–46° was obtained.

Found %: C 55.8; H 3.88; Si 21.7. $(C_6H_5SiO_{1.5})_x$. Calculated %: C 55.8; H 3.86; Si 21.7.

Preparation of poly(dimethylphenyl)siloxane. A mixture of 360 g of water and 180 g of toluene was charged into the hydrolyzer, fitted with cooling jacket, stirrer, thermometer and dropping funnel. Then a mixture of 68 g of dimethyldichlorosilane, 112 g of phenyltrichlorosilane and 180 g of dry toluene was added with constant stirring. The temperature of the mixture was kept constant at 20°. The mixture was stirred for 1 hour, after which the organic layer was separated from the water layer, washed with water until neutral, filtered, and the toluene removed from it by distillation. The obtained product was subjected to elemental analysis.

Found %: C 48.91; H 5.81; Si 29.01. $(C_8H_{11}O_2Si_2)_x$. Calculated %: C 49.23; H 5.64; Si 28.72.

Catalytic polymerization of polyphenylsiloxane. A 59.1% solution of 60 g of polyphenylsiloxane in toluene was placed in a round-bottomed flask fitted with dip tube and stirrer. Then a 39.36% NaOH solution (calculated as 0.9% on the polyphenylsiloxane) was added with vigorous stirring to the polycyclophenylsiloxane solution at 40°. The temperature during reaction was kept at 40°. Samples of the polymer were removed at periodic intervals and their relative viscosity as a 10% solution of the polymer in toluene was determined (by the Ostwald method). The reaction was stopped when a gel had formed. The experiments on the polymerization of the polyphenylsiloxane with 0.5 and 0.8% sodium hydroxide at 20° failed to lead to an increase in the viscosity of the product even after more than 100 hours.

Catalytic polymerization of poly(dimethylphenyl)siloxane. The experiments on the catalytic polymerization of the cohydrolysis products of dimethyldichlorosilane with phenyltrichlorosilane were run at 20°. The concentration of the polymer in toluene was 58.5%. Using the indicated conditions the experiments were run with a variable amount of sodium hydroxide (0.3, 0.5, 0.7 and 0.9% on the weight of polymer).

We also investigated the influence of the polymer concentration in toluene (using 0.3% NaOH) on the rates of gel formation and viscosity increase. The obtained data are shown in Figures 1–3.

SUMMARY

The catalytic polymerization of cyclic polyphenylsiloxanes, poly(dimethylphenyl)siloxanes and octamethylcyclotetrasiloxane was studied. It was established that the polydimethylphenylsiloxanes polymerize with greater ease than the polyphenylsiloxanes; octamethylcyclotetrasiloxane is polymerized when treated with small amounts of sodium hydroxide only on heating.

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Received February 2, 1957

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SOME DERIVATIVES OF MERCAPTOCAFFEINE AND MERCAPTOTHEOBROMINE

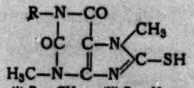
E. G. Berdichevskii, F. Iu. Rachinskii and E. K. Novoselova

The importance of sulfhydryl compounds in physiological processes is a universally studied subject. In this connection the mercapto derivatives of caffeine and theobromine are of especial interest.

Mercaptopurines and mercaptoxanthines were first obtained by E. Fischer [1], and on the basis of his method a patent was issued on the preparation of 8-mercaptocaffeine by the reaction of 8-chlorocaffeine with potassium hydrosulfide [2]. Literature data on the preparation and properties of 8-mercaptotheobromine are lacking. The synthesis of 8-mercaptotheophylline (1,3-dimethyl-2,6-dihydroxy-8-mercaptopurine) by heating the potassium salt of 1,3-dimethyluric acid with hydrogen sulfide at 150° under pressure is described in a patent [3].

A. M. Khaletskii and M. S. Eshman [4], who synthesized the thio analogs of theobromine by reacting the latter with phosphorus trisulfide, prepared 3,7-dimethyl-2,6-dithiopurine and came to the conclusion that of the two desmotropic forms possible for the dithiotheobromine, either the lactam or the lactim, preference should be given to the latter.

We repeated the synthesis of 8-mercaptocaffeine (I) under somewhat different conditions, using as starting reactants 8-bromocaffeine and an alcoholic solution of sodium hydrosulfide. 8-Mercaptotheobromine (II) was obtained in a similar manner.



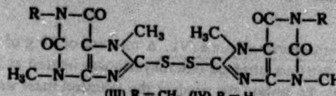
(I) R = CH_3, (II) R = H.

Mercaptocaffeine and mercaptotheobromine are practically insoluble in water, in contrast to their sodium salts (mercaptides). Based on preliminary data, these mercaptides are pharmacologically similar to caffeine and theobromine and can be used in medical practice in place of the soluble pharmacopoeia preparations of caffeine and theobromine. Of practical interest is the replacement of the diurethan of mercaptotheobromine, since the high alkalinity of the diurethan leads to its carbonization and reduces the solubility of the compound in water.

Bearing in mind that mercaptans tend to oxidize, we set out to protect the sulfhydryl group in order to increase the stability of the obtained compounds. We prepared some derivatives of mercaptocaffeine and mercaptotheobromine by replacing the hydrogen of the sulfhydryl group, on the assumption that in the organism it is possible for sulfides and disulfides to be converted into compounds containing the free sulfhydryl group.

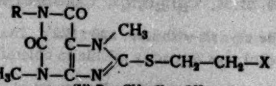
$$R{-}S{-}R + 2H \rightleftarrows R{-}SH + HR$$
$$R{-}S{-}S{-}R + 2H \rightleftarrows 2R{-}SH$$

The careful oxidation of mercaptocaffeine and mercaptotheobromine gave the corresponding disulfides (III) and (IV). Both of the latter compounds are practically insoluble in water, and for this reason are hardly suitable for pharmacological testing.



(III) R = CH$_3$, (IV) R = H

Reaction of the sodium salts of mercaptocaffeine and mercaptotheobromine with ethylene chlorohydrin gave respectively 1,3,7-trimethyl-2,6-dihydroxy-8-thiopurineethanol (V) and 3,7-dimethyl-2,6-dihydroxy-8-thiopurineethanol (VI), soluble to the extent of 1–4% in water at room temperature.



(V) R = CH$_3$, X = OH;
(VI) R = H, X = OH;
(VII) R = CH$_3$, X = NH$_2$;
(VIII) R = H, X = NH$_2$.

We also prepared the mercaptoamine derivatives in which the hydrogen of the sulfhydryl group was replaced by either caffeine (VII) or theobromine (VIII). The hydrochlorides of both 1,3,7-trimethyl-2,6-dihydroxy-8-thiopurineethylamine and 3,7-dimethyl-2,6-dihydroxy-8-thiopurineethylamine are readily soluble in water.

EXPERIMENTAL

1,3,7-Trimethyl-2,6-dihydroxy-8-mercaptopurine (I). To a suspension of 10 g of 8-bromocaffeine in 25 ml of anhydrous alcohol with vigorous stirring, in the cold, was added 50 ml of an 8% alcoholic solution of sodium hydrosulfide. The mixture was heated to the boil, and kept here until the odor of hydrogen sulfide disappeared. The precipitate was washed with anhydrous alcohol, dissolved in the minimum amount of water and, after treatment with activated carbon, was acidified with 10% HCl solution until acid to litmus. The obtained precipitate was washed with cold water, then with alcohol, and dried in a vacuum-desiccator. Yield 7.3 g (88%).

Found %: S 15.08, 14.62 (Messinger); N 25.01, 24.91 (Kjeldahl). $C_8H_{10}O_2N_4S$. Calculated %: S 14.16; N 24.78.

(I) was obtained as a white powder, with decomposition point around 250°; it is insoluble in water and organic solvents, and readily soluble in an equivalent amount of alkali with the formation of the mercaptide, which is readily soluble in water.

3,7-Dimethyl-2,6-dihydroxy-8-mercaptopurine (II). To a suspension of 10 g of 8-chlorotheobromine in 25 ml of anhydrous alcohol was added 65 ml of an 8% alcoholic solution of sodium hydrosulfide with vigorous stirring. Further treatment was the same as indicated above. Yield 6.8 g (about 68%).

Found %: S 16.14, 15.64; N 26.35, 26.77. $C_7H_8O_2N_4S$. Calculated %: S 15.09; N 26.41.

(II) was obtained as a microcrystalline powder, with decomposition point around 260°; it is insoluble in water and organic solvents. It forms the water-soluble mercaptide with an equivalent amount of sodium hydroxide.

Dicaffeine disulfide (III). Ten grams of the sodium salt of 8-mercaptocaffeine was dissolved in the minimum amount of water and then treated with the equivalent amount of 0.1 N aqueous iodine solution. The obtained precipitate was washed with water and then dried in a vacuum-desiccator. Yield 7.7 g (about 85%).

Found %: S 13.97, 13.91; N 25.31, 25.00. $C_{16}H_{18}O_4N_8S_2$. Calculated %: S 14.22; N 24.89.

(III) was obtained as a lemon-yellow powder, with decomposition point around 200°; it is insoluble in water, alcohol, ether and benzene; readily soluble in chloroform and in a large excess of aqueous sodium salicylate solution.

Ditheobromine disulfide (IV). Ten grams of the sodium salt of 8-mercaptotheobromine was treated with an equivalent amount of 0.1 N aqueous iodine solution, the same as in the preceding experiment. Yield 7 g (about 82%).

Found %: S 14.87, 14.70; N 26.25, 26.72. $C_{14}H_{14}O_4N_8S_2$. Calculated %: S 15.17; N 26.54.

(IV) was obtained as a yellow powder. Its decomposition point is around 285°; it is insoluble in water and organic solvents.

1,3,7-Trimethyl-2,6-dihydroxy-8-thiopurineethanol (V). A mixture of 10 g of the sodium salt of 8-mercaptocaffeine and 10 g of freshly distilled ethylene chlorohydrin was heated at 120° for 2 hours. The reaction mixture crystallized on cooling. To isolate the product the reaction mass was repeatedly treated with boiling anhydrous alcohol, from which colorless needle crystals deposited on cooling. Some more of the same substance was isolated from the mother liquor. Recrystallization from alcohol gave 8.5 g (about 80%) of crystalline product.

Found %: S 11.71, 11.88; N 21.59, 21.34. $C_{10}H_{14}O_3N_4S$. Calculated %: S 11.85; N 20.74.

(V) was obtained as colorless needle crystals with m.p. 120–122°. The compound is soluble at room temperature in water (up to 1%) and alcohol, and is readily soluble in chloroform.

3,7-Dimethyl-2,6-dihydroxy-8-thiopurineethanol (VI). Ten grams of the sodium salt of 8-mercaptotheobromine was mixed with 20.8 g of freshly distilled ethylene chlorohydrin; further treatment was the same as in the preceding experiment. Yield 8 g (about 73%).

Found %: S 11.95, 11.84; N 21.79, 21.81. $C_9H_{12}O_3N_4S$. Calculated %: S 12.50; N 21.87.

(VI) was obtained as a microcrystalline powder with m.p. 216–218°. It is soluble in water at room temperature (up to 1%); it is practically insoluble in organic solvents.

Hydrochloride of 1,3,7-trimethyl-2,6-dihydroxy-8-thiopurineethylamine (VII). Ten grams of the sodium salt of 8-mercaptocaffeine was added to 550 ml of an alcohol solution of 3.2 g of β-chloroethylamine, obtained from the corresponding hydrochloride. The mixture was heated with constant stirring on the boiling water bath for 5 hours, and then was immediately filtered. HCl gas was passed into the extremely cold filtrate. The resulting hydrochloride precipitate was filtered, washed with anhydrous alcohol, and dried in a vacuum-desiccator. Yield 10 g (about 81%).

Found %: S 9.96, 9.86; N 22.75, 22.74. $C_{10}H_{15}O_2N_5S \cdot HCl$. Calculated %: S 10.48; N 22.91.

(VII) was obtained as a fine white powder, with decomposition point around 249°. It is readily soluble in water at room temperature and in warm alcohol.

Hydrochloride of 3,7-dimethyl-2,6-dihydroxy-8-thiopurineethylamine (VIII). Ten grams of the sodium salt of 8-mercaptotheobromine was added to 320 ml of an alcohol solution of 3.4 g of β-chloroethylamine, obtained from the corresponding hydrochloride; further treatment was the same as in the preceding experiment. Yield 4 g (about 32%).

Found %: S 11.06, 11.41; N 23.13, 23.72. $C_9H_{13}O_2N_5S \cdot HCl$. Calculated %: S 10.98; N 24.01.

(VIII) was obtained as a white powder that sublimed at about 240° (with decompn.). It is readily soluble in water at room temperature, and is insoluble in organic solvents.

SUMMARY

Eight mercaptopurine derivatives were synthesized, of which six were obtained for the first time. Based on preliminary data, the pharmacological properties of the obtained compounds lie close to those of caffeine and theobromine.

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Received December 14, 1956

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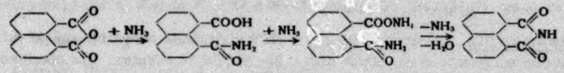
* Original Russian pagination. See C. B. Translation.

SYNTHESIS OF NAPHTHALIMIDE AND ITS DERIVATIVES

A. P. Karishin and D. M. Kustol

Incorrect conditions are given in the literature for the transformation of naphthalic anhydride and its derivatives to the corresponding imides. Some authors indicate that to obtain naphthalimide it is necessary to boil naphthalic anhydride for a long time (from 2 to 8 hours) with either aqueous or alcoholic ammonia solution [1–5], or to heat the mixture in an autoclave for 1–2 hours [6]. Methods are also described for the preparation of naphthalimide in which salts of naphthalic acid are heated with ammonium salts for a long time [7,8]. Similar methods were used to obtain 4-chloronaphthalimide, 4-bromonaphthalimide [9], 4-nitronaphthalimide [10], 4,5-dibromonaphthalimide and 4-bromo-5-chloronaphthalimide [11].

We established that naphthalic anhydride and its monohalo and mononitro derivatives are very easily converted to the corresponding imides when heated with 15–16% aqueous ammonia solution at 60–90° for 25–30 minutes. The yield of the corresponding imides reaches 98%. As our investigations show, the conversion of naphthalic anhydride under these conditions proceeds mainly through the ammonium salt of the monoamide of naphthalic acid, according to the following scheme

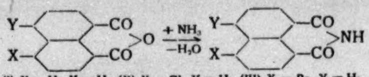


The formation of the ammonium salt of the naphthalic acid monoamide proceeds vigorously even at 50–60°. This salt is readily soluble in water, but is extremely unstable, and when the water solution is boiled it is almost completely (97%) converted to naphthalimide. Acidification of a water solution of the ammonium salt with hydrochloric acid gives the monoamide of naphthalic acid as a precipitate, which when boiled with water or on drying is 96% converted to naphthalic anhydride and 4% to naphthalimide.

The potassium salt of the naphthalic acid monoamide was isolated by us in the free state. This supports the statements made above regarding the existence in solution of the ammonium salt of the naphthalic acid monoamide as an intermediate product in the process for the formation of naphthalimide.

If naphthalic acid is taken to obtain naphthalimide, then its reaction with aqueous ammonia gives the diammonium salt, which when boiled in solution for 6 hours is converted to naphthalimide only to the extent of 70%. From this it follows that in order to obtain good yields of naphthalimide it is necessary to use naphthalic anhydride free of naphthalic acid as impurity, and also to use moderate heating (to avoid rapid loss of ammonia). To accomplish this we used naphthalic anhydride that had been recrystallized from boiling nitrobenzene, or else had been dried at 140–150° for 3–4 hours. Under the indicated conditions, anhydride that had been previously dried at 105–110° for 10 hours gives the imide in a yield not exceeding 84%. The reactions with the monosubstituted naphthalic anhydrides proceed in a similar manner.

The anhydrides of the dihalonaphthalic acids are converted with much greater difficulty to the corresponding imides. To obtain 4,5-dibromonaphthalimide it is necessary to use a large excess of aqueous ammonia and to heat at the boil for a long time (up to 2 hours). The 4,5-dichloro- and 4-bromo-5-chloronaphthalimides are obtained in good yields if the reaction is run in the presence of nitrobenzene. Apparently, the imides of the dihalonaphthalic acids are also formed directly through the ammonium salts of the monoamides, since the diammonium salts of the corresponding acids when boiled for 6 hours are converted to the corresponding imides only to the extent of 30–38%.



(I) X = H, Y = H; (II) X = Cl, Y = H; (III) X = Br, Y = H;
(IV) X = NO_2, Y = H; (V) X = Cl, Y = Cl; (VI) X = Br,
Y = Cl; (VII) X = Br, Y = Br.

EXPERIMENTAL

Naphthalimide (I). A mixture of 50 g of naphthalic anhydride and 80 ml of 16% aqueous ammonia solution was placed in a 200 ml two-necked flask, fitted with stirrer and reflux condenser. The flask with reactants was heated on the water bath for 30 minutes, in such a manner that vigorous boiling of the ammonia solution was avoided. The temperature of the mixture was gradually raised from 60 to 90°. The obtained mass was treated with 50 ml of water, stirred, filtered, the precipitate washed with water, and then dried at 105−110°. Yield 48.7 g, which is 97.9% based on taken, and 99% based on reacted naphthalic anhydride. The obtained naphthalimide proved to be free of the anhydride and other impurities, and did not have to be treated with soda. M.p. 299−300° (corr.), which did not change after repeated recrystallization from nitrobenzene. Acidification of the ammoniacal filtrate gave 0.73 g of naphthalic anhydride.

Naphthalimide is readily soluble in either 5% potassium hydroxide or sodium hydroxide solution at the boil. The corresponding potassium and sodium compounds crystallize from the solutions on cooling, and when treated with water are completely hydrolyzed to naphthalimide.

Potassium salt of naphthalic acid monoamide. A mixture of 5 g of naphthalic anhydride and 8 ml of 16% aqueous ammonia solution was heated at 50−60° for 25−30 minutes, then treated with 50 ml of water, and filtered. To the obtained solution of the ammonium salt of naphthalic acid monoamide was added 50 ml of 30% potassium hydroxide solution. The resulting precipitate was filtered, washed with 20 ml of water, then with 100 ml of alcohol, and dried at 105−110°.

Found %: N 5.43, 5.48. $C_{12}H_8O_3NK$. Calculated %: N 5.53.

4-Chloronaphthalimide (II). A mixture of 30 g of 4-chloronaphthalic anhydride and 45 ml of 16% aqueous ammonia solution was heated on the water bath at 60−90° for 30 minutes. The obtained slurry was treated with 30 ml of water and filtered. The precipitate was washed with water and dried. Yield of (II) 29.3 g (98%). The product was obtained completely pure; m.p. 302−303° (corr.). When boiled with 5% caustic alkali solutions it forms difficultly water-soluble compounds, which do not hydrolyze when treated with water.

4-Bromonaphthalimide (III) was obtained in the same manner as (II). From 30 g of 4-bromonaphthalic anhydride we obtained 29.25 g (98%) of (III). M.p. 296−297° (corr.). When treated with hot 5% caustic alkali solutions it forms difficultly water-soluble compounds, which hydrolyze with ease.

4-Nitronaphthalimide (IV) was obtained in the same manner as (II). From 30 g of 4-nitronaphthalic anhydride we obtained 29.15 g (97.5%) of (IV). The product is quite pure; m.p. 289−290° (corr.). It dissolves with comparative ease in aqueous caustic solutions, forming infusible compounds.

4,5-Dichloronaphthalimide (V). A charge of 20 g of 4,5-dichloronaphthalic anhydride, 20 ml of nitrobenzene and 160 ml of 16% aqueous ammonia solution was placed in a round-bottomed flask fitted with reflux condenser. The mixture was heated on the boiling water bath for 2 hours, after which it was transferred to a beaker, treated with 150−200 ml of 3% sodium hydroxide solution, and boiled until all of the nitrobenzene was removed. The precipitate was filtered and washed with water. It represented the water-insoluble, infusible sodium compound of (V). To isolate the free (V) the precipitate was transferred to a beaker, treated at the boil with 10% hydrochloric acid solution, cooled, filtered, and washed with water. Yield of (V) 17.5 g (88%). M.p. 371−372° (corr.). The compound crystallizes from nitrobenzene as yellow needles with m.p. 372−373° (corr.).

4-Bromo-5-chloronaphthalimide (VI) was obtained from the corresponding anhydride in the same manner as (V). Yield 65%; the compound crystallizes from nitrobenzene as yellow needles. M.p. above 365°. When treated with hot caustic alkali solutions it forms insoluble compounds, which are not hydrolyzed by water.

4,5-Dibromonaphthalimide (VII). A charge of 20 g of 4,5-dibromonaphthalic anhydride and 80 ml of 16% aqueous ammonia solution was placed in a round-bottomed flask and then heated on the boiling water bath for 2 hours. The obtained mixture was transferred to a beaker, 100 ml of 3% sodium hydroxide solution was added, and the mixture boiled for 10 minutes. The precipitate was filtered, washed with water, and dried. Yield of (VII) 19 g (95%). M.p. 341–342° (corr.). The compound crystallizes from nitrobenzene as fine yellow needles with m.p. 343–344° (corr.). When treated with boiling 5% potassium hydroxide solution the compound forms a water-insoluble compound, which in contrast to the sodium compound does not hydrolyze.

SUMMARY

The conditions for the transformation of naphthalic anhydride and its derivatives to the corresponding imides were studied. It was established that the transformation of the anhydride of naphthalic acid proceeds through the formation of an intermediate product—the ammonium salt of naphthalic acid monoamide.

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Received July 9, 1957

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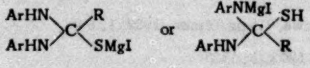
*Original Russian pagination. See C. B. Translation.

PREPARATION OF DISUBSTITUTED AMIDINES FROM DISUBSTITUTED THIOUREAS AND METHYLMAGNESIUM IODIDE

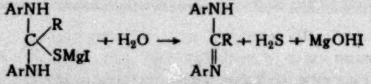
N. V. Koshkin

Several methods have been proposed for the preparation of amidines, of which the main ones for a long time have been those based on the reaction of ammonia with imino esters, imino chlorides or with the esters of orthocarboxylic acids. Recently some methods have been developed for the preparation of amidines from nitriles, cyanides and ammonium salts [1]. Disubstituted amidines of the aromatic series are also obtained in the reaction of organomagnesium compounds with diphenylcarbodiimides, from the anilides of aliphatic acids and aniline, or from a mixture of aliphatic acid and aniline [2].

In this paper we describe methods for the preparation of amidines from N,N'-disubstituted thioureas and methylmagnesium iodide, based on the addition of the organomagnesium compound to the double bond of either the >C = S or the >C =N – group, with the formation of an intermediate compound having the composition



Independent of whether it is the normal or the iso form of the thiourea that reacts with the organomagnesium compound, decomposition of the intermediate compound with water leads to amidine formation according to the equation



Due to the presence of the amidino group in isothioureas, the latter are also capable of forming amidines with sodiomalonic ester. For example, the reaction of N,N'-diphenylthiourea with sodiomalonic ester in benzene solution gives the diethyl ester of (N,N'-diphenylethenylamidine) dicarboxylic acid. Hydrolysis of this compound with alkali leads to the formation of N,N'-diphenylacetamidine

$$C_6H_5NC(NHC_6H_5)CH(COOC_2H_5)_2 \xrightarrow{2H_2O} C_6H_5NC(NHC_6H_5)CH_3 + 2CO_2 + 2C_2H_5OH$$

As a result of our work we prepared N,N'-diphenylacetamidine, N,N'-di(p-tolyl)- and N,N'-di(m-tolyl)-acetamidines, N,N'-di(o-anisidino)-acetamidine and N,N'-allylphenylacetamidine.

EXPERIMENTAL

Preparation of N,N'-diarylacetamidines from N,N'-diarylthioureas and methylmagnesium iodide. The N,N'-diaryl substituted thioureas were obtained for the experiments from the corresponding amines and ammonium thiocyanate by heating the reactant mixture in excess amine at 135–145° for 1.5–2 hours. Instead of ammonium thiocyanate it is also possible to use either thiourea or N-arylthioureas, heating them with aromatic amines, also taken in slight excess, at 145–170°.

An ether solution of methylmagnesium iodide was prepared from 2 g of magnesium and 10 g of methyl iodide in 30 ml of absolute ether. To the flask containing the organomagnesium compound was added in small portions, with mechanical stirring and cooling, 0.07 g-mole of the diarylthiourea, previously dried and pulverized to a fine powder. The addition of the diarylthiourea to the ether solution of the methylmagnesium iodide was accompanied each time by strong frothing of the reactant mixture. After all of the thiourea had been added, the reaction mixture was heated on the water bath for about an hour, after which the ether was distilled off, and the flask contents treated with small portions of either water or dilute hydrochloric acid containing cracked ice. If hydrochloric acid was used to decompose the organomagnesium compound, then the solution was made alkaline by treating with potash. The resulting precipitate of amidine was filtered, washed with water, and recrystallized from a small volume of alcohol.

N,N'-Allylphenylacetamidine. The allylphenylthiourea used for experiment was obtained from allyl mustard oil and aniline. An equimolar mixture of aniline and mustard oil was dissolved in two weight parts of ether and then allowed to stand for a day at room temperature. Coarse, yellow-colored crystals which proved to be insoluble in hot ether were obtained after such standing. After distilling off the ether, the precipitate was recrystallized from chloroform. M.p. 100–101°.

To obtain the allylphenylacetamidine, methylmagnesium iodide was prepared from 20 g of magnesium metal and 100 g of methyl iodide in 250 ml of absolute ether. The organomagnesium compound obtained in this manner was treated in small portions with 33.5 g of allylphenylthiourea with cooling, after which the flask was heated on the water bath for 30 minutes, the ether distilled off, and the flask contents after cooling treated with small portions of water. Aluminum chloride was added to the reaction flask to effect complete solution of the precipitated magnesium hydroxide. The obtained oily liquid was extracted with ether and dried over calcium chloride. Removal of the ether by distillation left an oily residue (13.8 g). Almost complete solution was obtained when the oily liquid was treated with 10% hydrochloric acid solution. The remaining tar was filtered and discarded.

Treatment of the hydrochloric acid solution of the amidine with alkali until alkaline again gave a yellowish oily liquid, readily extracted with ether.

The allylphenylacetamidine forms a salt with concentrated hydrochloric acid.

Found %: N 12.7. $C_{11}H_{14}N_2 \cdot HCl$. Calculated %: N 13.2.

The properties of the obtained N,N'-disubstituted amidines are listed in the table.

TABLE

Name of amidine	Formula of amidine	Melting point	Nitrogen content (in %)		Yield (based on the thiourea) (in %)
			found	calculated	
N,N'-Diphenylacetamidine	$C_{14}H_{14}N_2$	131.5°	13.13	13.32	75
N,N'-Di(p-tolyl)acetamidine	$C_{16}H_{18}N_2$	121	11.40	11.70	50
N,N'-Di(m-tolyl)acetamidine	$C_{16}H_{18}N_2$	104–105	11.26	11.70	60
N,N'-Di(o-anisidino)acetamidine	$C_{16}H_{18}O_2N_2$	137–138	10.15	10.36	52
N,N'-Allylphenylacetamidine (salt)	$C_{11}H_{14}N_2 \cdot HCl$	–	13.20	13.20	41

N,N'-Diphenylacetamidine from sodiomalonic ester and diphenylthiourea. The sodiomalonic ester was prepared from 12 g of malonic ester and 1.7 g of sodium metal in 150 ml of dry benzene with stirring and heating at 60–70°. The ester obtained in this manner was treated with 16 g of dry, finely divided diphenylthiourea, and the mixture heated for 6–8 hours at the boil. Then the benzene was distilled off, and the obtained precipitate was heated for 2 hours with 150–200 ml of cold-saturated alcoholic caustic solution. On conclusion of heating the solution was treated with water, and the obtained precipitate was filtered, washed with water, and recrystallized from alcohol. Yield 10 g. M.p. 131°.

Found %: N 13.20. $C_{14}H_{14}N_2$. Calculated %: N 13.32.

SUMMARY

1. Methods were proposed for the preparation of N,N'-diphenylacetamidine, N,N'-di(p-tolyl)acetamidine, N,N'-di(m-tolyl)acetamidine, N,N'-di(o-anisidino)acetamidine and N,N'-allylphenylacetamidine from methylmagnesium iodide and disubstituted thioureas.

2. N,N'-Diphenylacetamidine was also obtained by the reaction of sodiomalonic ester with diphenylthiourea.

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Leningrad Technological Institute of the Food Industry Received June 8, 1957

ACTION OF γ-RADIATION OF RADIOACTIVE COBALT (Co^{60}) ON AQUEOUS SOLUTIONS OF AROMATIC HYDROCARBONS

M. A. Khenokh and E. M. Lapinskaia

In aqueous solutions of organic compounds, in particular of hydrocarbons and their derivatives, ionizing radiation causes complex chemical transformations [1–7]. At the present time it is believed that the action of ionizing radiations on aqueous solutions is due to the radiolytic cleavage of the water into hydrogen atoms and free OH and O_2H radicals, with the formation of H_2 and H_2O_2 as the final products [8]. The oxidation of organic compounds that occurs here depends on the reaction of these radicals with the dissolved substance similar to the action of Fenton reagent ($H_2O_2 + Fe^{2+}$ mixture) [6a, 9]. Continuing our earlier studies of the effect of ionizing radiations [10, 11] and ultrasonic waves [12–15] on organic compounds, we subjected saturated aqueous solutions of chemically pure benzene and toluene, and of 0.01 M solutions of phenol, to the action of Co^{60} γ-rays (~ 2 curies) at 15 ± 2°.

To prepare the solutions we always used triple-distilled water. The experiments were repeated at least 3–5 times. The method of irradiation was described earlier [10a]. An SF-4 spectrophotometer was used to measure the absorption spectra, using a cuvette and a layer thickness of 5 mm. Formaldehyde [16] and the phenols [17, 18] were determined by the earlier described methods [13a]. The amount of radiation absorbed by the liquid was determined from the amount of $FeSO_4$ oxidized in 0.8 N H_2SO_4 solution in the presence of dissolved air. The Fe^{2+} concentration was determined by potentiometric titration with 0.01 N $KMnO_4$ solution. The original $FeSO_4$ concentration was $2.02 \cdot 10^{-3}$ M. The yield of oxidized iron was taken equal to 15.5 molecules per 100 ev [8].

Action of γ-rays on benzene solutions. The results obtained in the spectrophotometric measurement of irradiated benzene are shown in Fig. 1. An examination of the curves in Fig. 1 reveals that the exposure of benzene solutions to γ-rays results in an increased absorption of ultraviolet light. However, here the position of the maxima in the 230–260 mμ region is retained when compared with the spectrum of the original benzene solution, and new maxima do not appear. After irradiation the spectrum expands in the long-wave portion and embraces the region up to 280 mμ, in which connection sharp new absorption bands arise at 269 and 276 mμ. They indicate the formation of phenol [19]. In addition, a new absorption region appears (305–380 mμ) with a maximum at 348 mμ. The hydroxylation of benzene and the resulting formation of phenol are the result of the action of the free radicals that arise in the radiolysis of water under the influence of γ-rays [4]. The influence of the radiation dose on the formation of phenol in benzene solutions is shown in Fig. 2, from which it can be seen that the amount of phenol increases with increase in the dosage. The yield of phenol is 1.31 molecules/100 ev, which coincides with the literature data [20]. The oxidative processes that take place under the influence of γ-rays also cause decomposition of the benzene ring; formaldehyde was found in the reaction products. The amount of formaldehyde increases with increase in the radiation dose (Fig. 2). However, the yield of the product is very small–0.07 molecules/100 ev.

Similar changes in benzene solutions can also be obtained chemically by treating the benzene solution with Fenton reagent. According to the literature, Fenton solution causes the formation of phenol and polyphenols in benzene solutions [21]. To characterize the products that originate in a benzene solution when treated with Fenton reagent, we ran some experiments in which an increasing amount of H_2O_2 and a constant amount of $FeSO_4$ were added to a constant volume of benzene. The final volume of the mixture was made up to 10 ml by the addition of water. The solutions were allowed to stand for 24 hours at 15 ±2°, after which they were subjected

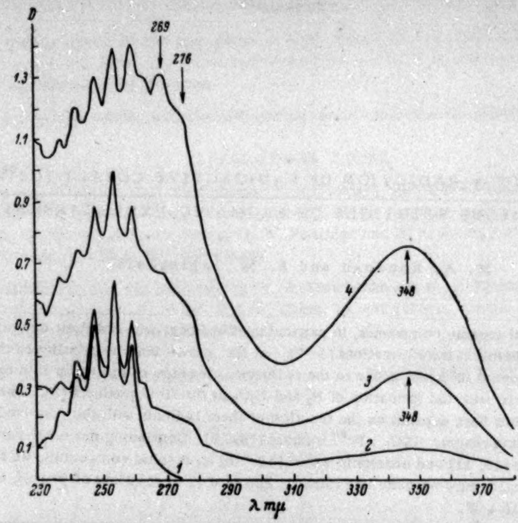

Fig. 1. Absorption spectra of benzene solutions irradiated with γ-rays.
1) Not irradiated, 2) irradiated with a dose of $0.9 \cdot 10^{19}$ ev/ml, 3) with a dose of $2.1 \cdot 10^{19}$ ev/ml, 4) with a dose of $3 \cdot 10^{19}$ ev/ml.

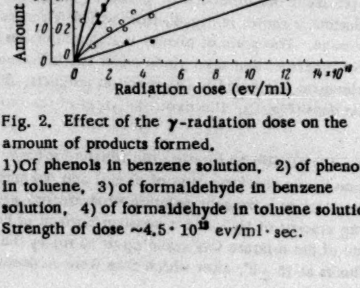

Fig. 2. Effect of the γ-radiation dose on the amount of products formed.
1) Of phenols in benzene solution, 2) of phenols in toluene, 3) of formaldehyde in benzene solution, 4) of formaldehyde in toluene solution. Strength of dose $\sim 4.5 \cdot 10^{13}$ ev/ml · sec.

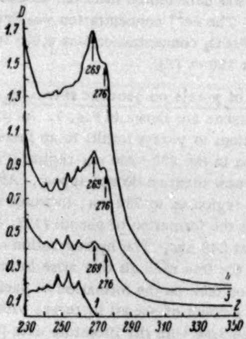

Fig. 3. Absorption spectra of benzene solutions subjected to the action of Fenton reagent ($5.5 \cdot 10^{-4}$ M Fe^{2+}).
1) Original benzene solution, 2) $5.9 \cdot 10^{-4}$ M. H_2O_2, 3) $14.7 \cdot 10^{-4}$ M. H_2O_2, 4) $29 \cdot 10^{-4}$ M. H_2O_2.

to spectrophotometry. The obtained data are shown in Fig. 3. From the curves it can be seen that the action of Fenton reagent, the same as that of γ-radiation, is to cause in benzene solutions an increase in the absorption intensity of ultraviolet light and the appearance of new absorption bands with λ_{max} at 269 and 276 mμ, characteristic for phenol. In contrast to the action of γ-rays, the action of H_2O_2 + Fe^{2+} failed to cause absorption of ultraviolet light in the region of greater wavelengths (305–380 mμ). As a result, in contradiction to the literature, our experiments indicate that the products, obtained in the action of γ-rays on aqueous solutions of benzene and those obtained by decomposition with H_2O_2 in the presence of $FeSO_4$ [6a], are not completely identical.

Action of γ-rays on toluene solutions. The curves for the absorption of ultraviolet light by toluene solutions are shown in Fig. 4. From Fig. 4 it can be seen that an increase in the total absorption occurs under the influence of γ-rays. Here the maxima at 261 and 268 mμ are also retained after irradiation. New bands do not appear in the 230–270 mμ region. Additional absorption arises in the 320–380 mμ region with λ_{max} at 353–354 mμ.

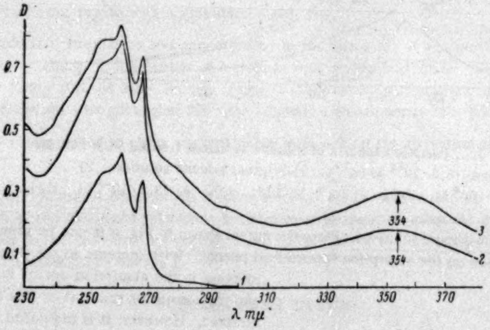

Fig. 4. Absorption spectra of toluene solutions irradiated with γ-rays. 1) Not irradiated, 2) irradiated with a dose of $1.46 \cdot 10^{19}$ ev/ml, 3) with a dose of $2.56 \cdot 10^{19}$ ev/ml. Strength of dose $6.1 \cdot 10^{13}$ ev/ml · sec

Chemical analysis indicates that toluene in aqueous solutions under irradiation suffers oxidative destruction with the formation of formaldehyde. The influence of the dose on the amount of formaldehyde formed as shown in Fig. 2, from which it can be seen that the amount of formaldehyde increases with increase in the radiation dose. The yield of formaldehyde is 0.17 molecules/100 ev. The formation of phenols here (Fig. 2) in a yield of 0.56 molecules/100 ev indicates that, together with decomposition processes, there occurs transformation of the toluene into a new compound with retention of the six-membered ring. Analysis shows that hydroxylation of the six-membered ring is accomplished with greater ease than is the formation of formaldehyde.

After irradiation of the toluene solutions, the same as in the case of benzene, the value of the pH dropped. A dose of $2.88 \cdot 10^{19}$ ev/ml caused the pH of the toluene solutions to drop from 6.0 to 3.98. A comparison of the yields of formaldehyde and phenolic compound in irradiated benzene and toluene solutions reveals that the profound destruction processes, causing the formation of formaldehyde, proceed with greater intensity in toluene than in benzene (Fig. 2); at the same time toluene suffers less hydroxylation than does benzene (Fig. 2). Evidently, this is due to the presence of the CH_3 group in toluene. The former, suffering chemical changes under the influence of ionizing radiation, diverts a part of the free radicals and in this way protects the six-membered ring from hydroxylation.

The action of Fenton reagent on toluene solutions revealed that the changes occurring here differ from those obtained in the exposure to γ-rays. The absorption spectra of the toluene solutions treated with Fenton reagent are shown in Fig. 5, from which it can be seen that with increase in the amount of H_2O_2 in Fenton reagent the action of the free radicals causes an increase in the absorption density in toluene solutions. Here the ultraviolet light absorption maxima at 261 and 268 mμ vanish, and new, ill-defined maxima appear at 248, 253 and 276 mμ. Absorption is absent in the 300–360 mμ region.

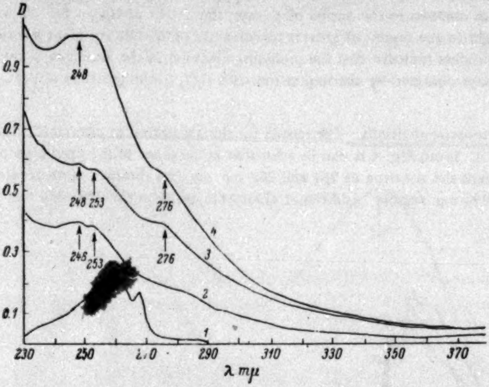

Fig. 5. Absorption spectra of toluene solutions treated with Fenton reagent ($5.5 \cdot 10^{-4}$ M Fe^{2+}). 1) Original toluene solution, 2) $5.9 \cdot 10^{-4}$ M. H_2O_2, 3) $14.7 \cdot 10^{-4}$ M. H_2O_2, 4) $23.5 \cdot 10^{-4}$ M. H_2O_2.

Action of γ-rays on phenol solutions. From the curves shown in Fig. 6 it can be seen that irradiation exerts very little influence on the absorption spectrum of phenol. With increase in the dose only slight increase in the absorption occurs in phenol solutions and the absorption maxima at 269 and 276 mμ are retained. However, it is indicated in the literature that phenol under the action of ionizing radiation can undergo transformation with the formation of quinone, catechol and other products [4]. As can be seen from Fig. 6, the absorption spectrum in the 230–300 mμ region does not reflect any changes in aqueous phenol solutions when exposed to γ-rays. Experiments with Fenton reagent revealed that increasing the H_2O_2 concentration in the reagent only led to a slight increase in the ultraviolet absorption without changing the characteristic spectrum of phenol. When the spectra of irradiated benzene, toluene and phenol (Figs. 1, 4 and 6) are compared, it can be seen that the least changes under the influence of γ-rays, and also of Fenton reagent, occur in the spectrum of phenol. This shows that changes in the absorption spectra of irradiated solutions of aromatic hydrocarbons depend on the character of the substituent in the six-membered ring.

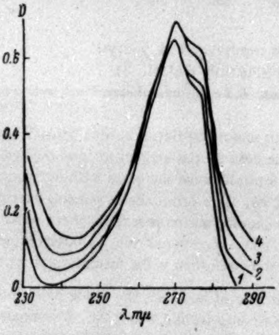

Fig. 6. Absorption spectra of phenol solutions irradiated with γ-rays. 1) Not irradiated, 2) irradiated with a dose of $4.92 \cdot 10^{19}$ ev/ml, 3) with a dose of $7 \cdot 10^{19}$ ev/ml, and 4) with a dose of $8.99 \cdot 10^{19}$ ev/ml. Strength of dose $6.1 \cdot 10^{15}$ ev/ml · sec.

Some authors believe it possible to assume that the mechanism of the chemical action of ionizing radiation in aqueous solutions is similar to that of the chemical influence exerted by ultrasonic waves [8a, 22–24]. The results of the present study also show that in irradiation the character of the changes in hydrocarbons is similar to their transformations under the influence of ultrasound [13a]. In both cases hydroxylation of the six-membered ring occurs in the hydrocarbon solutions, and also its destruction with the formation of formaldehyde. However a comparison of the spectra of irradiated and ultrasonically treated solutions of benzene and toluene reveals that γ-rays cause changes in these solutions that are sharply different from those evoked by ultrasonic treatment [13a]. Phenol solutions represent an exception which, judging by the spectra, proved to be equally stable toward both γ-rays and ultrasonic waves. The obtained material suggests that the chemical action of ionizing radiations differs from the reactions that proceed in aqueous solutions under the influence of an ultrasonic field. This conclusion is supported by earlier published studies [10–15].

SUMMARY

1. The action of the γ-radiation of radioactive cobalt (Co^{60}) on aqueous solutions of benzene, toluene and phenol was studied.

2. It was shown that when benzene solutions are exposed to γ-rays the six-membered ring suffers hydroxylation to give phenol in a yield of 1.31 molecules/100 ev, and also that it suffers destruction with the formation of formaldehyde in a yield of 0.07 molecules/100 ev. After irradiation the spectrum of benzene showed absorption in the 305–380 mμ region with a maximum at 348 mμ.

3. In toluene solutions irradiation was accompanied by the formation of a phenolic compound in a yield of 0.56 molecules/100 ev and of formaldehyde in a yield of 0.16 molecules/100 ev. Exposure to γ-rays failed to produce any changes in the 230–280 mμ region of the toluene spectrum, but after such exposure absorption appeared in the wavelength region 320–380 mμ with a maximum at 353–354 mμ.

4. Exposure to γ-rays failed to exert any noticeable influence on the absorption spectrum of phenol solutions.

5. The absorption spectra of benzene and toluene solutions that had been treated with Fenton reagent differ from the spectra of the irradiated solutions. In the case of benzene solutions the differences in the absorption bands appear in the 305–308 mμ region, while in the case of toluene solutions they are found in the entire region investigated (230–380 mμ).

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Received December 1, 1956

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*Original Russian pagination. See C. B. Translation.

CHANGE IN PROTEINS AND AMINO ACIDS UNDER THE INFLUENCE OF ULTRASONIC VIBRATIONS

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Earlier it had been shown that the exposure of aqueous solutions to ultrasonic vibrations causes the decomposition of high-molecular carbohydrates, saccharides, gelatin and amino acids [1–4]. Bearing in mind the scientific and practical importance assumed by ultrasonic vibrations (USV) in chemistry, it seemed of interest to expand the investigations on the influence of ultrasonics on proteins and amino acids. Literature sources indicate that proteins suffer various physicochemical changes when exposed to USV [5,6], while here amino acids suffer decomposition with the formation of aldehydes, ammonia and other compounds [3, 7, 8]. However, the published data are far from adequate to permit judging as to the new products that arise here, or as to the transformations suffered by these substances under ultrasonic treatment.

In this communication, being a continuation of our investigations on the influence exerted by ultrasonic vibrations [1–4, 9, 10] and by nuclear radiations [11, 12] on high-molecular compounds and their elementary units, we give the results of our experiments on the ultrasonic treatment of proteins, and of aliphatic and aromatic amino acids. For the experiments we took 25 ml portions of $2 \cdot 10^{-2} - 2 \cdot 10^{-3}$ M solutions of the amino acids and 0.5% solutions of the proteins: egg albumin (Kahlbaum), photogelatin, containing 0.054% ash after purification (by the Lebu method), and casein (by the Hammersten method), prepared using 0.1% soda solution, and exposed them at 38–40° to ultrasonic vibrations with a frequency of 435 kc.

To determine phenolic hydroxyls we used the method described in [10]; ammonia was determined by the diffusion method [13]. The relative viscosity was measured in an Ostwald viscosimeter at 25°, and the pH was determined using a glass electrode. An SF-4 spectrophotometer was used to take the absorption spectra. For the chromatographic analysis we used Factory No. 2 chromatographic paper. As solvent we used a mixture of n-butyl alcohol, acetic acid and water (5 : 4 : 1). As developer we used a 0.1% solution of ninhydrin in alcohol. For the quantitative chromatographing we used a 0.5% solution of ninhydrin in acetone [14]. The colored stains were cut out and extracted for about 5 hours in a test tube, in the dark, with 8 ml of 70% alcohol, previously saturated with $CuSO_4$. The obtained solutions were subjected to spectrophotometric measurement at λ 540 mμ, in a cuvette with a layer thickness of 5 mm, and a slit opening of 1.7 mm (as compared to alcohol in the reference cuvette). The change in the amino acid concentration in the solutions exposed to ultrasonic treatment was determined by the change in the absorption density, using that of the original amino acid concentration as a base. To quantitatively determine phenylalanine, tyrosine and tryptophan, we cut out from the chromatograms at the R_f level of the shown amino acid stains the corresponding adjacent portions, which were then eluted with 5 ml portions of 0.1 N HCl. The concentration of the aromatic amino acids was calculated from the decrease in absorption at λ_{max} in a cuvette with a layer thickness of 10 mm and using 0.1 N HCl as a comparison standard. The distribution of the aromatic amino acids on the chromatogram was also shown using an ultrachemiscope* with an UFS-2 filter. Histidine was determined using diazotized sulfanilic acid and spectrophotometric measurement of the solutions at λ 530 mμ (slit opening 1.4 mm) and a layer thickness of 5 mm [15]. Cysteine and cystine were determined by reduction with phospho-18-tungstic acid [13]. The spectrophotometric measurement of the solutions was made at λ 740 mμ [16] in a cuvette with a layer thickness of 4 mm and a slit opening of 0.04 mm. The amount of cystine, formed from cysteine under ultrasonic treatment, was determined from the difference in the concentrations, found when the reaction was

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[*] As in original—Publisher's note.

run in the presence of Na_2SO_3 and in its absence. Triple-distilled water was used in all of the experiments. The experiments were repeated at least 3–5 times. A description of the high-frequency generator used and the conditions of operation were given earlier [3,4].

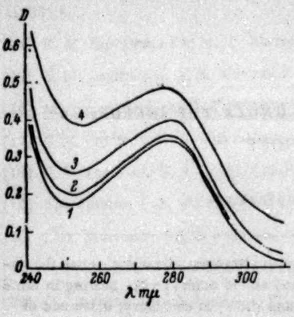

Fig. 1. Absorption curves of albumin solutions (c = 0.5%, d = 1 mm). 1) Not treated with ultrasonics, 2) treated with ultrasonics for 1 hour, 3) 3.5 hours, 4) 5 hours.

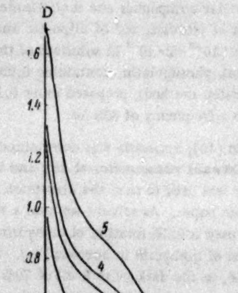

Fig. 2. Absorption curves of gelatin solutions (c = 0.5%, d = 4 mm). 1) Not treated with ultrasonics, 2) treated with ultrasonics for 3 hours, 3) 5 hours, 4) 7 hours, 5) 10 hours.

Action of ultrasonics on solutions of albumin, casein and gelatin. The results of the spectrophotometric measurement of ultrasonorated albumin solutions are shown in Fig. 1. An examination of the curves reveals that the protein absorption in the 230–300 mμ region increases with increase in the time of ultrasonic treatment. However, new absorption maxima do not appear, and the curves retain their original character. A similar change in the absorption was also observed when casein solutions are exposed to ultrasonic vibrations. The absorption spectrum of gelatin (Fig. 2), due to the absence of tryptophan and a reduced amount of other aromatic amino acids in it [17], differs sharply from the spectra of both albumin and casein. From Fig. 2 it can be seen that exposure of gelatin solutions to ultrasonic vibrations causes an increase in the absorption of ultraviolet light. Here after 3-hour exposure a bulge appears on the absorption curves in the 250–290 mμ region, which then levels out with further ultrasonic exposure.

The spectrophotometric analysis data obtained for the solutions of albumin, casein and gelatin do not permit judging as to the nature of the new compounds formed during ultrasonic exposure; however, the obtained curves do serve as evidence that changes occur in protein molecules when they are exposed to USV. In order to determine more accurately the physicochemical changes that take place in protein solutions when exposed to ultrasonics, we investigated the effect of USV on gelatin. From the curves in Fig. 3 it can be seen that in the case of 0.5 and 1% gelatin solutions, exposed to ultrasonic action, the viscosity drops. The character of the curves indicates that the viscosity strives to reach a certain state, which does not change when the time of ultrasonic exposure is increased. For the 0.5% gelatin solution such a state is attained after 2-hour exposure to USV, and for the 1% solution it is attained after exposure to USV for 7–8 hours. A second measurement of the viscosity, made for the 0.5% gelatin solutions after being kept for 16 hours at 19 ± 2°, revealed that even after aging the viscosity of the gelatin that had been exposed to ultrasonics for 1 hour was 52% less than the viscosity of the original solution. The irreversible decrease in the viscosity indicates that together with the mechanical effect, exposure to ultrasonic vibrations causes chemical processes, leading to the decomposition of protein molecules.

Earlier it was established that the cleavage of ammonia and the formation of formaldehyde occur here [3]. Ultrasonic treatment of gelatin solutions is

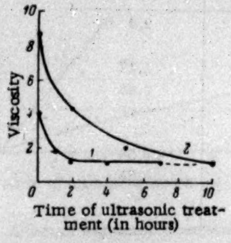

Fig. 3. Change in the relative viscosity of gelatin when exposed to ultrasonic treatment. 1) 0.5% solution, 2) 1% solution.

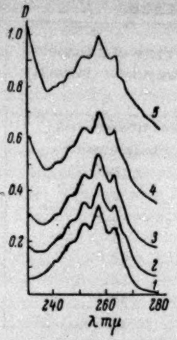

Fig. 4. Absorption curves of phenylalanine ($c = 2 \cdot 10^{-2}$ M, $d = 1$ mm). 1) Not treated with ultrasonics, 2) treated with ultrasonics for 0.5 hour, 3) 1 hour, 4) 2 hours, 5) 4.5 hours.

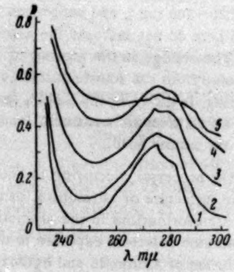

Fig. 5. Absorption curves of tyrosine solutions ($c = 2.2 \cdot 10^{-3}$ M, $d = 1$ mm). 1) Not treated with ultrasonics, 2) treated with ultrasonics for 2 hours, 3) 5 hours, 4) 10 hours, 5) 17 hours.

accompanied by a decrease in the pH, but to a lesser extent than in the case of pure water. After exposure to ultrasonics for 4 hours the pH decrease in water was 48.2% of the original value (pH 6.2), whereas when 0.25, 0.5 and 1% gelatin solutions were exposed to ultrasonics for the same length of time the pH decrease was respectively 25.8, 16.1 and 11.3%. The decrease in pH shown by water solutions when exposed to ultrasonics is due to the oxidative effect of cavitation, causing the formation of HNO_2 and HNO_3 [3,5]. As the protein concentration is increased the buffering action of the solution is also increased, which apparently hinders change in the pH.

Action of ultrasonics on amino acid solutions.

To obtain a better idea of the transformations that take place in proteins when exposed to ultrasonic waves, we investigated the action of ultrasonics on amino acids. Since the absorption shown by proteins in the ultraviolet portion of the spectrum is mainly due to the presence of aromatic amino acids in the macromolecules, it seemed of interest to first determine the effect of USV on the change in the absorption of the indicated amino acids. The results obtained when ultrasonorated solutions of phenylalanine ($2 \cdot 10^{-2}$ M), tyrosine ($2.2 \cdot 10^{-3}$ M) and tryptophan ($2 \cdot 10^{-3}$ M) were subjected to spectrophotometric measurement are shown in Figs. 4–6. The curves show that the absorption of ultraviolet light in phenylalanine (Fig. 4) and tyrosine (Fig. 5) solutions increases as the time of exposure to ultrasonic treatment is increased. However, here new absorption maxima are not formed. The absorption curves probably also reflect the absorption of light by the products formed during ultrasonic treatment. Consequently, the measured absorption density is apparently the sum of the absorption shown by the still undecomposed molecules of the original substance and the newly formed compounds.

The absorption spectra of phenylalanine and tyrosine, isolated by chromatographing the ultrasonically treated solutions, revealed a reduction in the absorption of ultraviolet light, which permitted the conclusion that the amino acids had undergone partial decomposition. Quantitative data on the change in the concentrations of these amino acids are shown in the Table.

TABLE

Time of ultrasonic treatment (in hours)	Concentration of amino acid (in mole/liter)		
	phenylalanine ($\times 10^2$)	tyrosine ($\times 10^3$)	tryptophan ($\times 10^3$)
Not treated with ultrasonics	2.0	2.2	2.0
3	–	–	1.17
5	–	–	0.65
6.5	–	1.76	–
8	1.7	–	–
10	–	1.39	0.54
15	–	–	0.35
17	–	1.12	–
19	1.2	–	–

In tryptophan solutions, the same as in the case of phenylalanine and tyrosine, new absorption maxima fail to be formed as the result of exposure to ultrasonics. However, the absorption drops in solutions of this amino acid as the time of exposure to ultrasonic treatment is increased (Fig. 6). Evidently, the destruction products of tryptophan either have a slight absorption value or do not absorb at all in the indicated region of the spectrum (230–300 mμ), and consequently the substances formed here do not increase the absorption of the solutions. The change in the amount of tryptophan, separated from the transformation products by chromatographing, is shown in the Table, from which data it is obvious that ultrasonic treatment leads to decomposition of the amino acid.

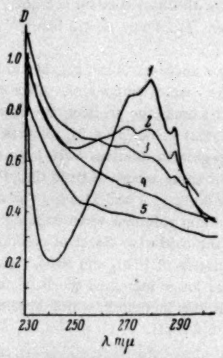

Fig. 6. Absorption curves of tryptophan solutions ($c = 2 \cdot 10^{-3}$ M, d = 1 mm). 1) Not treated with ultrasonics, 2) treated with ultrasonics for 3 hours, 3) 5 hours, 4) 10 hours, 5) 15 hours.

The oxidative processes, occurring in aqueous solutions under the influence of ultrasonics, cause various chemical transformations in the aromatic amino acids. In phenylalanine solutions exposure to ultrasonics results in the evolution of ammonia and hydroxylation of the benzene ring. Figure 7 shows that both deamination and the formation of phenolic hydroxyls increase with increase in the time of exposure to USV. This means that together with destruction of the NH_2 group, phenylalanine is converted to a new compound with retention of the six-membered ring. The decomposition of aromatic amino acids when exposed to ultrasonics is accompanied by the formation of new products, giving a color test with ninhydrin. The chromatograms of phenylalanine ($R_f = 0.65$) solutions that had been treated with ultrasonics for 10 hours showed five stains with $R_f = 0.50$ and 0.40. Ultrasonic exposure for 15 hours caused the additional formation of stains with $R_f = 0.30$ and 0.08. Chemical changes in tyrosine ($R_f = 0.51$) solutions after exposure to USV for 5–17 hours resulted in the appearance of a stain with $R_f = 0.30$ on the chromatogram of the amino acid. The eluate, obtained from the paper cut out from the corresponding portion of the chromatogram at the level of this colored stain, absorbed ultraviolet light in the 270–300 mμ region with the maximum absorption at 282 mμ. On increasing the time of exposure of the tyrosine solution to ultrasonics the density of ultraviolet light absorption in the eluate decreased, indicating decomposition of the new compound formed in the ultrasonic treatment of tyrosine. Identification of the stains appearing on the chromatograms will be the subject of further studies.

Histidine suffers decomposition when exposed to ultrasonics. Exposure of $1 \cdot 10^{-2}$ M solutions of the amino acid to USV for 5, 10 and 15 hours caused decomposition of the histidine to the extent of 18, 38 and 53%, respectively. It is the imidazole ring that is destroyed here, since the reaction with diazobenzenesulfonic acid steadily gave a weaker color, characteristic for the presence of the imidazole ring, as the time of histidine exposure to ultrasonics was increased.

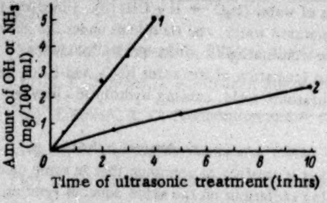

Fig. 7. Effect of ultrasonic treatment on the formation of phenolic hydroxyls (1) and deamination (2) in $2 \cdot 10^{-2}$ M phenylalanine solutions.

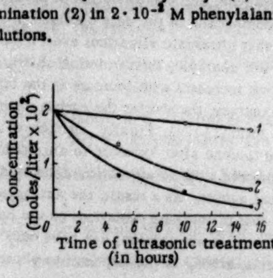

Fig. 8. Decomposition of aliphatic amino acids when exposed to ultrasonics. 1) alanine, 2) valine, 3) n-leucine.

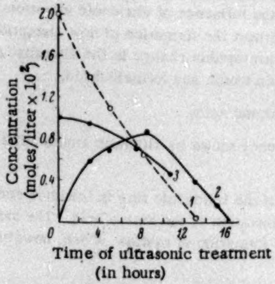

Fig. 9. Effect of ultrasonic treatment on the change in the concentration of cysteine and cystine. 1) decomposition of cysteine, 2) formation of cystine from cysteine, 3) decomposition of cystine.

The chemical processes occurring during ultrasonic exposure also produce changes in the solutions of aliphatic amino acids. The curves in Fig. 8 show that the extent of amino acid decomposition increases as the time of exposure to ultrasonics is increased. The longer the chain in the amino acid, the more extensive is the decomposition of the amino acid with the formation of ammonia and formaldehyde [3]. With the same exposure time, for example after 10 hours of ultrasonic treatment, the decrease in the amounts of alanine, valine and n-leucine was respectively 9, 59 and 75% of the original. The chromatographic analysis results revealed that the destruction of aliphatic amino acids is accompanied by the formation of new products, giving stains when the paper is developed with ninhydrin.

Rupture of the CO–NH bond occurred when 0.013 M solutions of hippuric acid were exposed to ultrasonic treatment for 10–15 hours. The chromatograms of solutions treated in this manner showed a stain, from its position corresponding to that of glycine. The presence of the latter was confirmed by chromatographing the ultrasonorated solutions in two different solvents (butyl alcohol, acetic acid and water, and phenol that had been saturated with water in an atmosphere of ammonia). Together with hydrolysis, hippuric acid also suffered hydroxylation during ultrasonic treatment. After exposure to USV for 3 and 6 hours the solutions of hippuric acid were found to contain respectively 1.7 and 3.1 mg of OH groups per 100 ml of solution.

Exposure to USV also causes chemical transformations in solutions of sulfur-containing amino acids. The results obtained in the ultrasonic treatment of solutions of cysteine and cystine are shown in Fig. 9, from which it can be seen that the decomposition of cysteine increases with increase in the time of exposure to ultrasonics, and reaches nearly 100% after exposure for 13 hours (Curve 1). The oxidative processes that occur here cause transformation of the cysteine to cystine. Curve 2 (Fig. 9) shows that the formation of cystine increases at first, and then, as the time of exposure is increased, it decreases. The latter suggests that USV exerts a destructive action on cystine. This is also supported by Curve 3 in Fig. 9.

To establish the influence exerted by the HNO_2, HNO_3 and H_2O_2 [5], formed in water when the latter is exposed to ultrasonic treatment, on the decomposition of amino acids, we prepared solutions of the latter using water that had been previously exposed to USV for 15 hours. After being kept at 38–40° for 10–15 hours the solutions were subjected to chromatographic analysis. However, except for the stains showing the location of the deposited amino acids, the chromatograms failed to show any new stains. Evidently, destruction of aliphatic amino acids is not caused by H_2O_2, HNO_2 and HNO_3, but instead depends on the oxidative action exerted by the free radicals arising in the ultrasonic field from the decomposition of water ($H_2O \rightarrow H + OH$) [5]. However, in the case where hippuric acid solutions were prepared using ultrasonorated water, and then kept under the above indicated conditions, analysis revealed that a stain appeared on the chromatogram, from the R_f "evidence" corresponding to free glycine. This permits the conclusion that the formation of the acids HNO_2 and HNO_3 also exerts an influence on the decomposition of hippuric acid in an ultrasonic field, causing hydrolytic cleavage of the –CO–NH– bond.

The results of the present study show that the action of USV causes substantial chemical changes in solutions of proteins and amino acids. The obtained material makes it possible to conclude that in some cases the effect of ultrasonic treatment is similar to the action of ionizing radiations on the same aqueous systems. Thus, in both cases the change in the spectra of proteins and aromatic amino acids has a similar character [12b]. When exposed to ultrasonic waves, the same as when exposed to γ-rays, amino acids show ammonia evolution, destruction of the carbon chains with cleavage of the carbon as formaldehyde, and hydroxylation of the six-membered ring in the case of aromatic amino acids [3, 12a, 12b]. A comparison of the data obtained in ultrasonic treatment with that obtained using ionizing radiation also shows that ultrasonic vibrations exert a specific influence on solutions of amino acids and other compounds [2b, 11b]. For example, the formation of NH_3 and H_2CO in the destruction of amino acids when exposed to ultrasonic waves increases with increase in the length of the amino acid chain [3], whereas in the case of radiolysis, on the contrary, the shorter the carbon chain, the greater the amount of the above indicated decomposition products formed [12a]. Finally, differences in the character of the absorption spectra of aqueous solutions of benzene and toluene after exposure to ultrasonics [10] or to the action of γ-rays [12b] permit assuming that the six-membered rings of aromatic amino acids suffer dissimilar transformations under the influence of the mentioned physical agents. As a result, the analogy cited by some authors between the chemical action of ultrasonic waves and that of ionizing radiations on the basis that free radicals [5] are formed in aqueous solutions under their influence, in our opinion, can have only limited significance, since it was experimentally shown that the products, arising in the exposure to ultrasonic waves and to nuclear radiation, are different.

SUMMARY

1. The action of ultrasonic vibrations was studied on solutions of albumin, casein, gelatin, and aliphatic and aromatic amino acids. It was shown that protein solutions under the influence of ultrasonic vibrations show increased absorption of ultraviolet light in the 230–300 mμ region without the formation of new absorption bands. In gelatin solutions the action of ultrasonic vibrations caused irreversible change in the viscosity, a fall in pH, and decomposition of the molecule with the formation of ammonia and formaldehyde.

2. Ultrasonic vibrations cause the decomposition of aromatic amino acids.

3. It was shown that the longer the chain, the greater the tendency shown by aliphatic amino acids to decompose under the influence of ultrasonic vibrations.

4. The action of ultrasonic vibrations leads to decomposition of the imidazole ring in histidine and to rupture of the CO–NH bond in benzoylglycine (hippuric acid) with liberation of the amino acid. The oxidative action of ultrasonic vibrations causes destruction of cysteine with the formation of cystine which, however, on further ultrasonic treatment also suffers decomposition.

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Received February 7, 1957

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*Original Russian pagination. See C. B. Translation.

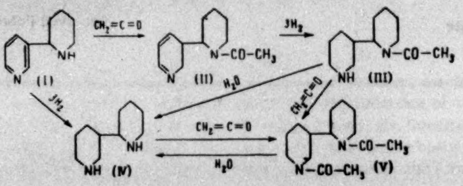
REACTION OF KETENE WITH NITROGEN-CONTAINING BASES

V. ACETYLATION OF BIPIPERIDINE WITH KETENE

Iu. V. Svetkin

In the previous communication [1] it was shown that ketene can be successfully used for the acetylation of certain alkaloids. Especially good results are obtained if the reaction is run with the additions of either acetic acid or water. Later this method was extended to derivatives of the bipiperidine series, the reactivity of which toward ketene has not been studied up to now. In addition, it seemed interesting to incidentally touch upon the subject of the structure of ammodendrine. As is known, this alkaloid was first isolated by Orekhov and Proskurnina [2] from Ammodendron conollyi Bge. Ammodendrine is a secondary base, has one double bond, and an acetyl radical. Orekhov and Proskurnina [3], by hydrogenating ammodendrine obtained dihydroammodendrine, which was then methylated. Subsequent saponification of the methyl derivative showed the position of the acetyl group, whereas the position of the ethylene bond was determined only tentatively. Recently Schopf and Braun [4] in decomposing N-acetylisotripiperidine with hydriodic acid obtained ammodendrine, and in this way rigidly proved the position of the double bond in this alkaloid.

We subjected anabasine and its derivatives to hydrogenation and incidentally studied dihydroammodendrine. The whole cycle of the transformations involved is shown in the scheme below.



The product (III) (monoacetylbipiperidine) obtained by us had constants different from those of dihydroammodendrine, and this served as additional evidence that the formula proposed by Schopf and Braun for ammodendrine is correct. On the other hand, as the result of our work it was established that ketene in the presence of CH_3COOH readily acetylates bipiperidine and its derivatives.

EXPERIMENTAL

Hydrogenation of acetylanabasine (II). Acetylanabasine was obtained by the acetylation of anabasine (I) with ketene in the presence of acetic acid. The hydrogenation of acetylanabasine was run in the following manner. Ten grams of acetylanabasine with b.p. 198–200° (5 mm) and $n^{20}D$ 1.5541 was added to 200 ml of boiling anhydrous alcohol. Then 24 g of sodium metal was added to the reaction mixture through the reflux condenser. On conclusion of reaction the mixture was treated with hydrochloric acid until acid, and then the alcohol was removed by vacuum-distillation. Yield of N-monoacetyl-α,β-bipiperidine 1.3 g (12.6%).

B.p. 130–132° (5 mm), $n^{20}D$ 1.5132, d^{20}_4 1.0928, MR_D 57.85; calculated 60.77.

Found %: C 68.07; H 10.36; CH_3CO 20.89. $C_{12}H_{22}ON_2$. Calculated %: C 68.53; H 10.54; CH_3CO 20.47.

In a similar manner the hydrogenation of anabasine (I) gave α,β-bipiperidine (IV), which had b.p. 113–114° (5 mm) and m.p. 66–68°.

Saponification of N-acetyl-α,β-bipiperidine (III). One gram of monoacetylbipiperidine (III) was dissolved in 10 ml of water and 20 ml of concentrated hydrochloric acid. The mixture was boiled under reflux on the water bath. The solution after cooling was neutralized with concentrated alkali and the bipiperidine was extracted with ether. The ether was distilled off, and the residue was vacuum-distilled. B.p. 113–114° (5 mm), m.p. 66–68° (from ether). These constants are in good agreement with the literature data for bipiperidine.

Preparation of N,N'-diacetyl-α-β-bipiperidine (IV). One gram of monoacetylbipiperidine (III) was placed in a four-necked flask, fitted with reflux condenser, mechanical stirrer, gas inlet tube and thermometer, and then 10 ml of acetone, containing 0.1 ml of glacial acetic acid, was added. Ketene was bubbled into the reaction mixture for 10 minutes. The amount of acetone consumed in pyrolysis was 30 ml. Evolution of heat during reaction was not observed. Then the reaction products were transferred to a small Wurtz flask, and the acetone removed by distillation. The residue was vacuum-distilled. The fraction with b.p. 232–235° (5 mm) was collected; yield 0.8 g.

n^{20}_D 1.5322, d^{20}_4 1.1316, MR_D 68.85; calculated 70.35.

Found %: C 66.20; H 9.32. $C_{14}H_{24}O_2N_2$. Calculated %: C 66.63; H 9.52.

Acetylation of bipiperidine. One gram of bipiperidine with m.p. 66–68° was acetylated with ketene in a solution of 20 ml of acetone, containing 0.1 ml of glacial acetic acid. In heating the reaction mixture no noticeable change was observed. The amount of acetone consumed in pyrolysis was 60 ml. After reaction we isolated N,N'-α,β-bipiperidine with b.p. 232–235° (5 mm) and n^{20}_D 1.5322. Yield 0.7 g.

SUMMARY

1. The previously unknown monoacetyl- and diacetylbipiperidines were synthesized.

2. The position of the acetyl group in ammodendrine was determined.

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Received December 24, 1956

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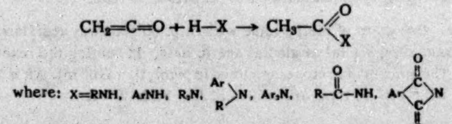
* Original Russian pagination. See C. B. Translation.

THE REACTION OF KETENE WITH NITROGEN-CONTAINING BASES

VI. THE MECHANISM OF THE ACETYLATION OF AMINES WITH KETENE

Iu. V. Svetkin

At the present time it is considered in the literature that the acetylation of amines by ketene proceeds in one stage by the equation



$$CH_2{=}C{=}O + H{-}X \rightarrow CH_3{-}C\begin{matrix}{=}O\\ {-}X\end{matrix}$$

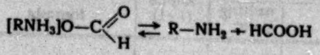
However, this hypothesis disagrees with experimental fact. As is known, in most cases the reaction of carbomethylene with various classes of organic compounds, including amines, is possible only in the presence of catalysts. In addition, a series of chemists have shown that ketene does not react directly with amines [1−6]. Finally, this treatment of the problem cannot be considered correct from purely theoretical considerations as it originates formally from general ideas on the ethylene bond.

In previous work we showed [3,7] that the acetylation of some amines with ketene in the presence of water proceeded through the formation of the corresponding acetates. Consequently, in this case also ketene does not react directly with amines (as in the examples given previously [1−7]) and thus the mechanism of this reaction remains unexplained at the present time. Therefore, if the formation of acetates as intermediates in the acetylation of amines were definitely established, it would be very valuable for determining the mechanism of this reaction. The secondary bases selected for this work were some which give salts with acetic acid that may be isolated readily in the form of stable crystalline substances. On the other hand, it is known that amines and acids in a 1 : 1 molecular ratio give the corresponding ammonium bases. We used this property to determine whether the ketone acted as a dehydrating agent in the second stage of the acetylation. Then when the ketene reacted with these onium compounds, one would expect the formation of the corresponding anilides by the scheme

$$[R{-}NH_3]OCOR' \xrightarrow[-H_2O]{CH_2=C=O} R{-}NH{-}CO{-}R' + CH_3COOH.$$

Using a number of amine salts, it was shown that they reacted with ketene to give only aceto derivatives. It follows from this that the ketene does not act as a dehydrating agent in the second stage of the reaction.

On the other hand, there is the possibility that molecular dissociation of the quaternary ammonium compounds occurs in nonpolar solvents. In order to determine if the reaction proceeded through this stage, we made use of the properties of the mixed anhydride of formic and acetic acid, which may be used as a formylating agent [8−11]. Therefore, in the case of the acetylation of amine formates with ketene, one would expect the formation of the corresponding formyl derivative if this dissociation did occur.



$$[RNH_3]O-C\begin{smallmatrix}O\\ H\end{smallmatrix} \rightleftarrows R-NH_2 + HCOOH$$

$$HCOOH + CH_2=C=O \rightarrow CH_3COOCOH$$

$$RNH_2 + CH_3COOCOH \rightarrow RNH-CH=O + CH_3COOH$$

However, when ketene was passed into a solution of these salts, the formyl derivative was not formed. Acetanilides were the sole reaction products. Thus, this course of the reaction may also be excluded.

Finally, it could be postulated that ketene reacted with amine acetates in nonpolar solvents through the hydrogen atom located at the nitrogen, which would give an acetate of the substituted amide type. Due to the sharp fall in the basicity constants, acid would be eliminated and the acetyl derivative formed.

$$[RNH_3]OCOCH_3 + CH_2=\overset{+}{C}=\overset{-}{O} \rightarrow [R-\overset{+}{N}H_2COCH_3]\overset{-}{O}OCCH_3$$

$$[R\overset{+}{N}H_2COCH_3]\overset{-}{O}OCCH_3 \rightarrow RNH-COCH_3 + CH_3COOH$$

When the amines were acetylated with ketene in the presence of water or other polar solvents, the acetates formed underwent the following dissociation.

$$[R-NH_3]OCOCH_3 \rightleftarrows [RNH_3]^+ + CH_3CO\overset{-}{O}$$

This indicated that ketene can react only with ions containing hydrogen.

$$[RNH_3]^+ + CH_2=\overset{+}{C}=\overset{-}{O} \rightleftarrows [RNH_2COCH_3]^+$$

$$[R-NH_2COCH_3]^+ + \overset{-}{O}OCCH_3 \rightleftarrows R-NH-COCH_3 + CH_3COOH$$

Thus the acetylation proceeds by an ionic type of chain mechanism, subject to the rules of acid catalysis.

EXPERIMENTAL

General acetylation method for secondary amines and salts. Into a four-necked flask, fitted with a mechanical stirrer, a reflux condenser, a thermometer and a gas inlet tube, was placed 60 ml of solvent and 5 g of amine. The calculated amount of water for an amine, water ratio of 1:1, was added. The contents of the flask were stirred for several minutes and then the introduction of ketene was begun. After 8–10 minutes, the separation of a voluminous precipitate was observed. Some of the crystals were removed, washed with anhydrous acetone and dried in a vacuum desiccator and their melting point determined to identify the acetates of the starting amines. The rest of the salt was acetylated with ketene until the acetates dissolved completely. After this the addition of ketene was stopped, the solvent partially distilled off and the melting points of the anilides precipitated were determined.

The acetylation of previously prepared salts was performed in dry solvents. The rest of the method was the same as the previous one. The acetylation of salts in water proceeded considerably faster. The amine salts which were not crystalline substances were prepared by mixing equimolar amounts of the amine and the appropriate acid in anhydrous solvents. The formylation was by the methods in [8–11]. In all cases we obtained appropriate amine derivatives, which agreed with the data of previous authors completely; therefore we do not present the results of this part of the work. The results of experiments on acetylation are listed in the table.

SUMMARY

A mechanism is proposed for the acetylation of amines by ketene in the presence of water or acids. This reaction obeys the usual rules of acid catalysis.

Expt. no.	Starting material		Added to amine (1 : 1)	Acetyl derivative		Yield (in %)
	formula	melting point		formula	melting point	
1	$(C_6H_5)(C_6H_{11})NH$	b.p. 139—141° (9mm)	H_2O	$(C_6H_5)(C_6H_{11})NCOCH_3$ *	68—69°	92
2	$[(C_6H_5)(C_6H_{11})NH_2]OOCCH_3$	154	—	$(C_6H_5)(C_6H_{11})NCOCH_3$	the same	90
3	$[(C_6H_5)(C_6H_{11})NH_2]OOCC_3H_7$	—	C_3H_7COOH	$(C_6H_5)(C_6H_{11})NCOCH_3$ **	the same	92
4	$(C_6H_{11})_2NH$	b.p. 123—125° (17mm)	H_2O	$(C_6H_{11})_2NCOCH_3$ *	102°	93
5	$[C_6H_{11})_2NH_2]OOCCH_3$	64—65°	—	$(C_6H_{11})_2NCOCH_3$	the same	90
6	$[(C_6H_{11})_2NH_2]OOCC_3H_7$	—	C_3H_7COOH	$(C_6H_{11})_2NCOCH_3$ **	the same	91
7	$(C_6H_5)(\alpha\text{-}C_{10}H_7)NH$	62	CH_3COOH	$(C_6H_5)(\alpha\text{-}C_{10}H_7)NCOCH_3$	115°	93
8	$(C_6H_5)(\beta\text{-}C_{10}H_7)NH$	108	CH_3COOH	$(C_6H_5)(\beta\text{-}C_{10}H_7)NCOCH_3$	93	92
9	$[\beta\text{-}C_{10}H_7NH_3]OOC_3H_7$	—	C_3H_7COOH	$(\beta\text{-}C_{10}H_7)NHCOCH_3$ **	134	94
10	$(o\text{-}CH_3C_6H_4NH_3)OOCH$	61—64	—	$o\text{-}CH_3C_6H_4NHCOCH_3$ ***	110	95
11	$(o\text{-}CH_3C_6H_4NH_3)OOCCH_2Cl$	95	—	$o\text{-}CH_3C_6H_4NHCOCH_3$ ****	the same	94
12	$(o\text{-}CH_3C_6H_4NH_3)OOCC_3H_7$	—	C_3H_7COOH	$o\text{-}CH_3C_6H_4NHCOCH_3$ **	the same	92
13	$(p\text{-}CH_3C_6H_4NH_3)OOCCH_2Cl$	101	—	$p\text{-}CH_3C_6H_4NHCOCH_3$ ****	the same	83
14	$(p\text{-}CH_3C_6H_4NH_3)OOCC_6H_5$	52—53	—	$p\text{-}CH_3C_6H_4NHCOCH_3$ *****	the same	90

* Acetates were formed in the first stage of acetylation.

** The butyryl derivative was not found.

*** The formyl derivative was not found.

**** The chloroacetyl derivative was not found.

***** The benzoate was not found.

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Received December 24, 1956

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* Original Russian pagination. See C. B. Translation.

A STUDY OF THE COMPARATIVE REACTIVITY OF THE HYDROXYL GROUPS IN CELLULOSE*

V. THE DISTRIBUTION OF METHOXY GROUPS IN PARTLY-METHYLATED CELLULOSE OBTAINED IN AN ALKALINE MEDIUM AT DIFFERENT CONCENTRATIONS OF ALKALI

V. Derevitskaia, M. Prokof'eva and Z. Rogovin

An earlier work [1] gave the results of a study of the reactivity of the hydroxyl groups in cellulose in the reaction involving the formation of alkali cellulose by treatment of the cellulose with 18% alkali and subsequent methylation. In the present work, alkali cellulose was prepared by treating cellulose with alkali solutions of different concentrations – 8, 13 and 40%. The alkali cellulose formed was pressed out until its weight was 3 times that of the original cellulose and washed free from adsorbed alkali using dry isobutyl alcohol. The washed alkali cellulose was methylated. In certain cases the alkali cellulose, pressed out to 3 times its weight, was methylated without being washed.

TABLE 1

Specimen No.	Alkali concentration (%)	Alkali cellulose composition, γ (from Na)	OCH_3 content (%)	γ for methylcellulose
1	8	46	4.7	26.3
2	8	48	4.8	27.0
3	8	49	4.1	23
4	13	101	15.5	87.5
5	13	105	16.9	91
6	13	98.5	14.8	87.5
7	13	95.5	—	—
8	40	100.9	16.0	90.8
9	40	94.2	15.6	88.7
10	40	108.7	18.6	105

TABLE 2

Specimen no.	Alkali concentration (%)	OCH_3 content (%)	γ for methylcellulose
1	8	5.68	32.2
2	8	3.16	18
3	8	3.53	26
4	13	14	79
5	13	11.6	66.2
6	13	14.8	83.5
7	13	16.3	92
8	40	30.8	173
9	40	29.5	169
10	40	30.9	174

Table 1 gives characteristic data for the washed alkali cellulose and corresponding methylcellulose specimens obtained.

It can be seen from the data given in Table 1 that as the alkali concentration is changed from 13 to 40%, the value of γ for the alkali cellulose remains unchanged and is equal to approximately 100. When the alkali cellulose is methylated, the methylcellulose obtained has a value for γ which is very close to the value of γ for the alkali cellulose. When the alkali concentration is reduced to 8%, the washed alkali cellulose has a lower value for γ, and when this is methylated, the methylcellulose obtained has a value for γ which is approximately one-half of the value of γ for the original alkali cellulose.

Unwashed alkali cellulose obtained by the action of 8–13% alkali, like that obtained by the action of 18% alkali [1], gives, on methylation, methylcellulose with values of γ (Table 2) which are very close to the values of γ for the methylcellulose obtained by methylation of the corresponding washed alkali celluloses.

When cellulose is treated with 40% alkali and the alkali cellulose obtained is subsequently methylated without being washed, the methylcelluloses obtained have considerably higher values of γ than those for methylcelluloses obtained from washed alkali cellulose. The value of γ for this methylcellulose is much higher than the value of γ for all the other methylcelluloses given above. This indicates that the value of γ for alkali cellulose obtained by treating cellulose with 40% alkali is higher than the value of γ as determined by the direct method, in which the alkali cellulose is washed with alcohol, so that alcoholysis is unavoidable. It is known from data obtained by an indirect method that the quantity of combined alkali in alkali cellulose obtained by treatment with 40% alkali is ~2 times greater than the combined alkali content in alkali cellulose obtained by treatment with 13–18% alkali [2].

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* 64th communication in the series "A Study of the Structure and Properties of Cellulose".

TABLE 3

Specimen no.	Alkali concentration (%)	γ for methylcellulose	Triphenylmethylcarbinol content in the methylcellulose trityl ether (%)	γ for methylcellulose trityl ether	No. of OCH_3-groups on 6tn C-atom	Z•
1	8	96.5	53.0	71.0	29.0	1.2
2	13	87.5	55.2	76.0	24.0	1.3
3	13	87.5	53.6	72.1	27.9	1.1
4	13	91.0	54.2	73.5	26.5	1.2
5	40	88.7	57.5	86.3	13.8	2.7
6	40	90.0	57.0	83.2	16.8	2.2
7	40	105.0	57.5	86.3	13.8	3.3

In order to study the distribution of methoxy groups in the chain unit of the methylcelluloses obtained, the number of free primary hydroxyl groups was determined by the tritylation method, and in a number of cases an additional method involving nitration with subsequent iodination was used. The results of the study of the methylcelluloses obtained from washed alkali cellulose are given in Table 3.

A study of the methylcelluloses obtained from unwashed alkali cellulose gave analogous results. Thus tritylation of methylcellulose with $\gamma = 92$ (Specimen 7, Table 2) yielded a trityl ether with $\gamma = 71.5$ and a corresponding value for $Z = 1.11$.

The data in Table 3 show that when the concentration of alkali is increased from 13 to 40% the value of Z increases sharply, i.e. as the alkali concentration is increased to 40% the process of alkali cellulose formation and subsequent methylation takes place more selectively.

TABLE 4

Specimen No.	γ for the methylcellulose	Total γ for the methylcellulose nitrate $\gamma OCH_3 + \gamma ONO_2$	γ for the methylcellulose iodonitrate γ_I
3, Table 3	87.5	286.5	72.5
6, Table 3	90.0	297.0	88.3

In a number of cases, in addition to the tritylation method, a method involving nitration of the methylcelluloses and subsequent iodination was used to determine the number of primary hydroxyl groups.

It can be seen from a comparison of the data in Tables 3 and 4 that the results obtained are in good agreement with those obtained by the tritylation method.

• Z— the ratio of the average number of methoxy groups attached to 1 secondary carbon atom to the number of methoxy groups attached to the primary carbon atom.

EXPERIMENTAL

Cotton was used as the starting material [1]. The alkali cellulose was prepared by treating the cellulose with an alkali solution of the required concentration (8, 13 and 40%) at 20° for 1 hour with a liquor ratio of 20 : 1, after which it was wrung out to 3 times its weight. The preparation of the washed alkali cellulose, the methylation of the alkali cellulose with methyl iodide, and the determination of the number of free primary hydroxyl groups by tritylation of the methylcelluloses or by iodination of the methylcellulose nitrates, were carried out as described earlier [1].

SUMMARY

1. A study has been made of the distribution of methoxy groups in partly-methylated cellulose obtained by the action of methyl iodide on alkali cellulose prepared in alkali with concentrations varying from 8 to 40%.

2. The distribution of methoxy groups in the methylcellulose changes as the concentration of the alkali used for the preparation of the alkali cellulose changes from 13 to 40%. The reaction involving alkali cellulose formation and subsequent methylation proceeds more selectively with the secondary hydroxyl groups at an alkali concentration of 40%.

3. When unwashed alkali cellulose, obtained by the action of 40% alkali solution, is methylated, the methylcellulose obtained has considerably higher values of γ (169-179) than the methylcelluloses obtained by methylation of the corresponding washed alkali cellulose (88-105). It is evident that the value of γ for this alkali cellulose is higher than the value of γ obtained by the direct method, in which alcoholysis of the alkali cellulose takes place.

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Received January 17, 1957

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*Original Russian pagination. See C.B. Translation.

A STUDY OF THE COMPARATIVE REACTIVITY OF THE HYDROXYL GROUPS IN CELLULOSE*

VI. THE DISTRIBUTION OF METHOXY GROUPS IN THE PRODUCTS OF THE METHYLATION OF Na CELLULOSE ALCOHOLATE

V. Derevitskaia, M. Prokof'eva and Z. Rogovin

Sodium cellulose trialcoholate was first prepared by Scherer and Hussey [1], who treated cellulose with a solution of metallic sodium in liquid ammonia. They measured the volume and rate of evolution of hydrogen in this reaction and established that the amount of hydrogen corresponded to the formation of sodium cellulose trialcoholate, noting at the same time that one mole of hydrogen was liberated rapidly while the two others were liberated very slowly. The reaction between cellulose and metallic sodium in liquid ammonia was next studied by Shorygin and Makarova-Zemlianskaia [2]. They also obtained sodium cellulose trialcoholate, but did not observe a sharp difference in the rate of evolution of hydrogen throughout the reaction. The alcoholate obtained was methylated to yield methylcellulose with $\gamma = 100$. An attempt to determine the distribution of methoxy groups in the chain unit of the methylcellulose obtained, by methods involving tritylation and hydrolysis with subsequent separation of the osazones, was unsuccessful. Timmel [3] used the reaction involved in the formation of sodium cellulose alcoholate in liquid ammonia in his studies of the structure of cellulose. It can be seen from data given in this work on the measurement of the rate of evolution of hydrogen that the first mole of hydrogen is evolved at the highest rate.

TABLE 1

Specimen No.	Quantity of Na (in moles per mole of cellulose)	Time required for the evolution of the first mole of hydrogen τ_1 (seconds)	$\tau_1^*:\tau_2:\tau_3$
1	3	365	1:2.2:19
2	3	332	1:2.15:18.5
3	9	237	1:2.:16.7
4	1+1+1	1426	1:1.92:11.5

*τ_1 taken as unity.

Thus in spite of the fact that the reaction involved in the formation of sodium cellulose alcoholate in liquid ammonia has been studied by a number of workers, there are no data at present on the reactivity of the hydroxyl groups in cellulose in the reaction with metallic sodium. In the present work an attempt has been made to arrive at a solution to this problem.

The preparation of sodium cellulose alcoholate and the measurement of the rate of hydrogen evolution were carried out in the apparatus and using the method described by Shorygin and Makarova-Zemlianskaia [2]. The experiments were carried out on pulped cotton sulfite cellulose and on viscose rayon. Measurements were made of the time taken for the evolution of each mole of hydrogen in the reaction between cellulose and sodium at different sodium concentrations. In some of the experiments the sodium was added at the start of the experiments in an amount corresponding to 3 moles per mole of cellulose or in large excess, while in other experiments the sodium was added in 3 separate portions. The rate of reaction varied with the amount of sodium added for reaction, but the ratio of the times required for the evolution of the first, second and third moles of hydrogen ($\tau_1:\tau_2:\tau_3$) remained practically constant (Tables 1, 2).

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* 65th communication in the series "A Study of the Structure and Properties of Cellulose".

TABLE 2

Specimen No.	Quantity of Na (in moles per mole of cellulose)	Time required for the evolution of the first mole of hydrogen τ_1 (seconds)	$\tau_1{}^*:\tau_2:\tau_3$
1	3	155	1:1.6:7.8
2	9	125	1:1.68:7.55
3	9	144.5	1:1.57:7.6
4	1+1+1	512	1:1.71:8.1
5	1+1+1	539	1:1.64:7.05

* τ_1 taken as unity.

The total rate of reaction and the ratio $\tau_1:\tau_2:\tau_3$ depend on the nature of the cellulose specimen. The rate of evolution of the first mole of hydrogen in the reaction with metallic sodium in the case of viscose rayon (Table 1) exceeds the rate of evolution of the third mole by a factor of 16-18, whereas in the case of the pulped cellulose (Table 2) the factor is 7-8. This is evidently explained by the difference in the total reaction rates: the rate of formation of sodium cellulose trialcoholate in the reaction between sodium and cellulose pulp is 3-5 times greater than the rate of this reaction for viscose rayon. The influence of the total reaction rate on the ratio of the rates at which the three hydroxyl groups in cellulose react has been shown in a number of examples. Thus in the acetylation of cellulose [4] in the presence of catalysts, when the rate of reaction is high, the ratio of the reactivities of the primary and secondary hydroxyl groups in this reaction is 2.5 : 1, whereas at a low rate of acetylation without catalyst, this ratio is 16 : 1.

TABLE 3

Specimen No.	Starting material	γ for the sodium cellulose alcoholate	γ for the methylcellulose	γ for the methylcellulose trityl ether	Number of OCH_3--groups on the 6th C atom
1	Cotton	100	53	99	1
2	"	100	48	98.5	1.5
3	"	100	68	97	3
4	Viscose rayon.	100	68	100	0
5	" "	100	50	102	0
6	" "	100	89	101	0
7	Cellulose pulp	100	102	95	5
8	" "	200	130	64	36
9	" "	200	131	67.8	32.2
10	" "	200	143	58	42

We have assumed that the considerable difference in the rates of evolution of the 3 moles of hydrogen in the reaction between cellulose and metallic sodium is determined chiefly by the different reactivities of the hydroxyl groups of cellulose in this reaction. In order to confirm this assumption, it was necessary to study the distribution of sodium in the chain unit of the sodium cellulose alcoholate. Since the direct study of sodium cellulose alcoholate is difficult due to its low stability, specimens of sodium cellulose alcoholate with $\gamma = 100-$ -200 were methylated and a study made of the distribution of methoxy groups in the methylcelluloses obtained. Before the methylation process, the ammonia was completely removed from the reaction medium by blowing dry nitrogen through it, and the sodium cellulose alcoholate was methylated with methyl iodide in the same reaction vessel at room temperature for 12 hours. This yielded methylcellulose with a very low methoxy group content (1.6–2%). In subsequent experiments the ammonia was not removed completely or in some cases was extracted from the sodium cellulose alcoholate using dry toluene.

In order to obtain methylcellulose with a higher degree of methylation, some of the methylcellulose specimens were treated a second time with a solution of sodium in liquid ammonia and then with methyl iodide. This yielded methylcelluloses with $\gamma = 30 - 143$, in which the number of free primary hydroxyl groups was determined by the tritylation method. The results of the tritylation showed (Table 3) that the formation of sodium cellulose alcoholate with γ up to ≈ 100 and subsequent methylation take place exclusively with the secondary hydroxyl groups. In the methylcellulose with $\gamma \approx 100$, practically all the primary hydroxyl groups are free.

Further reaction involving the formation of sodium cellulose alcoholate with $\gamma > 100$ takes place with the primary hydroxyl groups.

The data obtained on the distribution of methoxy groups in the products of the methylation of sodium cellulose alcoholate confirm the assumption made above, that the difference in the rates of evolution of the 3 moles of hydrogen in the reaction involved in the formation of sodium cellulose alcoholate is caused chiefly by the difference in the affinities of the three hydroxyl groups toward sodium.

EXPERIMENTAL

The starting materials used were scoured cotton [5], viscose rayon and pulped sulfite cellulose [5].

The sodium cellulose alcoholate was prepared by treating the cellulose with a solution of metallic sodium in liquid ammonia in the apparatus and using the method described in [2]. The ammonia was dried thoroughly and redistilled twice. No hydrogen was evolved when the metallic sodium was added, indicating that no moisture was present. The sodium was introduced into the reaction vessel either all at once at the start of the reaction or in portions at separate stages of the reaction. The hydrogen liberated was collected in a eudiometer over acidified water. The end of the reaction was established from the disappearance of the characteristic blue color of the solution of sodium in ammonia and the end of the hydrogen liberation. The time required for the liberation of each milliliter of hydrogen was measured using a stopwatch, in order to determine the rate of hydrogen evolution. The sodium cellulose alcoholate was methylated using sodium iodide (26–35 moles per mole of the alcoholate) in the same apparatus at room temperature for 12 hours. Before the methylation, the ammonia was evaporated from the reaction vessel until the sodium cellulose alcoholate was only slightly wet with ammonia, after which the methyl iodide was added. In some cases the ammonia was extracted from the sodium cellulose alcoholate using toluene. The methylation products were washed with hot and then with cold methanol and acetone, dried and analyzed.

The methods used for the determination of the methoxy group content, the tritylation of the methylcellulose and the analysis of the trityl ether have been described earlier [5].

SUMMARY

1. A study has been made of the distribution of methoxy groups in partly-methylated cellulose obtained from sodium cellulose alcoholate.

2. The formation of sodium cellulose alcoholate with γ up to 100 and subsequent methylation take place only with the secondary hydroxyl groups of the cellulose; further reaction involving the formation of sodium cellulose alcoholate with $\gamma > 100$, and methylation of the product, proceeds with the primary hydroxyl group of the cellulose.

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Received January 17, 1957

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*Original Russian pagination. See C.B. Translation.

THE KINETICS OF OXIDATION OF CELLULOSE BY NITROGEN PEROXIDE ACCORDING TO DATA OBTAINED FROM THE ABSORPTION SPECTRA OF THE PRODUCTS

I. N. Ermolenko and M. M. Pavliuchenko

The product of oxidation of cellulose by nitrogen peroxide possesses a number of valuable properties: good solubility in alkali, the ability to form insoluble salts with polyvalent metals, etc. It is recommended for use in medicine for various purposes [1–4]. This product was obtained by Shorygin and Rogovin and their co-workers [6], while studying the nitration reaction. Its properties have been studied by a number of authors [6–10, 12, 15, 24, 25]. The reaction mechanism of the oxidation of cellulose by nitrogen peroxide has been investigated by McGee and co-workers [11], Nabar and Padmanabhan [16], etc.

In spite of a large amount of work connected with the oxidation of cellulose by nitrogen peroxide the kinetics of this reaction has been studied very inadequately and the hypotheses put forward on the mechanism of the process have not been substantiated [13]. The application of new, particularly spectroscopic, methods has enabled us to establish a number of new and very interesting facts connected with the mechanism of the reaction. On the basis of an investigation of the spectra of organic nitrites, their solutions, the oxides of nitrogen in the free and adsorbed states, nitric and nitrous acids, oxidized cellulose before and after pumping out the samples under vacuum, heating and treating with solvents, we have shown that among the macromolecular products from the oxidation of cellulose with NO_2, in addition to substances containing carboxyl and carbonyl groups, a considerable quantity of cellulose nitrite occurs [5]. For the determination of its content in the oxidation products we used the magnitude of the optical density at λ 365 mμ; the carboxyl group was determined by the change in the optical density at λ 250 mμ, and the carbonyl group at λ 280 mμ [5, 19].

EXPERIMENTAL

Samples of cellophane were oxidized by nitrogen peroxide at 31° for periods of 10, 20, 45, 140, 180, 285 and 450 minutes in a specially constructed apparatus, using a method developed by us. A detailed description of the method has already been published [20].

Results of the spectrophotometric study of the samples obtained, in the region 270–400 mμ, are given in Fig. 1.

As we have shown [5], the absorption in this region indicated the formation of nitrite. The intensity of the absorption band changes with time, denoting a change in the cellulose nitrite content. The thickness of the films was measured by means of a vertical IZV-1 gauge. The cellophane used had a thickness of 29.7 μ. Assuming that the optical density of a layer of constant thickness for the same wave line (365 mμ) is proportional to the nitrite content, we constructed a graph of the variation of optical density, and hence also of the nitrite content, with time of oxidation. The nitrite content grows initially, then a maximum is reached after 45 minutes at 25°, after which it falls to a constant value.

Films of oxidized cellophane, after washing with water and drying, were re-examined spectrophotometrically. The absorption bands characteristic of nitrites then disappeared completely. This would explain the results of Rowen et al. [18] who examined the absorption spectra of samples oxidized with NO_2 only after treatment with water, no nitrite absorption bands being observed. The spectra of water-washed products, in the region 210–270 mμ, are given in Fig. 2. An intense absorption maximum is seen at about 220 mμ. A small absorption band at 280 mμ is seen in Fig. 4. As we have discussed previously [5, 19], the presence of the absorption maxima at 220 and 280 mμ is connected with the presence of carboxyl and carbonyl groups in the product. The carboxyl group content was also determined by the calcium acetate method and the carbonyl group content by the hydroxylamine method [29]. The quantity of carbonyl groups in the reaction products was 1–1.5%. The change in carboxyl and carbonyl group content, and also the equivalent weight of the product, can be estimated from the absorption curves as is done for many organic substances [21]. It is sufficient for our purpose to know the relative change in carbonyl group content during the course of the reaction. In this case the spectroscopic method gives very accurate and reliable results. For the determination of the absolute value of the carboxyl group content by the spectroscopic method, it is necessary to determine the carboxyl content of at least one sample by chemical methods. The curves of variation of optical density D, at λ 220 mμ, with time of oxidation have the same form as the curves of variation of carboxyl content with reaction time, obtained by the calcium acetate method. A carboxyl group content of about 19% corresponds to about 1.5 carboxyls to 2 elementary cellulose-chain segments. The limiting carboxyl content is reached in less than 500 minutes oxidation.

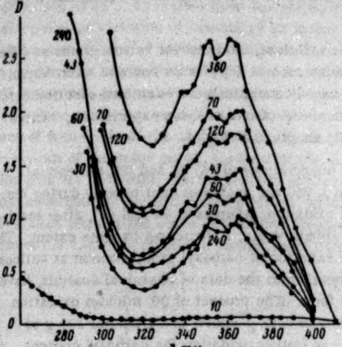


Fig. 1. Absorption spectra of cellulose films oxidized by nitrogen peroxide at 31°. [Reaction times (in minutes) shown on diagram on the corresponding curves.]

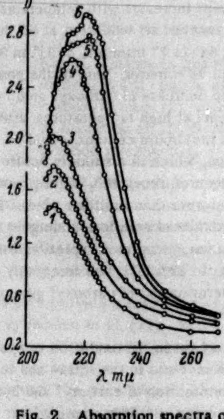
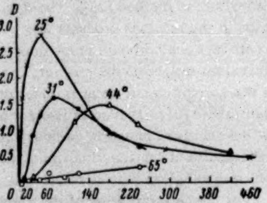


Fig. 2. Absorption spectra of products of oxidation of cellulose at 25°, obtained after treating the products with water and drying. Reaction time (in minutes): 1) 2, 2) 15, 3) 60, 4) 120, 5) 207, 6) 300.

A study of the effect of temperature on the rate and mechanism of the oxidation reaction is of interest, both from the practical and theoretical points of view. We carried out a series of experiments on the oxidation of cellulose at 25, 31, 44 and 65°. In each series the samples were oxidized for a different time. The absorption curves from the experiments carried out at 25 and 44° had the same form as the curves of Fig. 1; however at higher temperature the separate maxima in the region 320–400 mμ became less sharp and the total absorption decreased. At long oxidation times a slight shift in the separate absorption maxima in the short wave region was observed.

Determination of the combined nitrogen content in our samples, by the Kjeldahl method, showed that the curves of variation of combined nitrogen with time, have the same form as those for the change in nitrite content. This is in conformity with our views on the large role of cellulose nitrite in the oxidation. A considerable proportion of combined nitrogen in the product corresponds to nitrite, and not to nitrate as a number of investigators assume. For the lower alcohols the formation of nitrites by the action of nitrogen peroxide, both in the vapor and liquid phases, has been established [27]. Fig. 3 shows curves of the variation of optical density D at λ 365 mμ with oxidation time, at 25, 31, 44 and 65°. From comparison of these curves with one another it is seen that the nitrite content falls with increasing temperature and the time interval from the beginning of the experiment to the attainment of the maximum increases: at 25° after 45 minutes, at 31° after 70 minutes and at 44° after 180 minutes. While the maximum nitrite content depends on the temperature, its limiting content (at long reaction times) is approximately the same at the different temperatures. Oxidation of cellulose for 242 minutes at 65° gives no maximum in the optical density–reaction time curve.



Time (in minutes)

Fig. 3. Variation of optical density of films at λ 365 mμ with time of oxidation at 25, 31, 44 and 65°. (Temperature of experiments shown on the corresponding curves.)

The cellulose, oxidized for various times at different temperatures was kept for 24 hours in water vapor. After drying, the samples were examined spectroscopically. The results of one of these experiments, carried out at 44°, are given in Fig. 4.

At temperatures of 16, 25 and 31° the optical density at λ 250 mμ increases continuously during the course of oxidation, whereas at 44 and 65°, after reaching a maximum value, it decreases to some extent. The curves of variation of carboxyl group content at various temperatures, from the data of chemical analysis, have the same form. The product of 90 minutes oxidation at 65° contains 0.13 g-equiv. of COOH per 100 g of cellulose; on further oxidation the carboxyl content decreases a little. The product of 242 minutes oxidation at the same temperature still contains 0.12 g-equiv. of COOH per 100 g of cellulose. In the case of oxidation at lower temperatures (16, 25 and 31°) no lowering of carboxyl group content is observed after the attainment of a certain limiting value. Oxidation at 25° for 280 minutes gives a product containing up to 0.18 g-equiv. of COOH per 100 g of cellulose, and at 31° for 240 minutes—up to 0.23 g-equiv. The initial rate of formation of carboxyl groups increases with temperature. Thus, for example, a content of 0.08 g-equiv. of COOH per 100 g of cellulose is reached on oxidation at 65° in 15 minutes, at 44° in 27 minutes, at 31° in 36 minutes and at 16° in 70 minutes. One of the possible causes of the decrease in carboxyl group content in experiments at high temperatures, after attainment of the maximum content, could be decarboxylation, which in a strongly acidic medium in the presence of excess NO_2 takes place at a lower temperature than in dilute acids. It is known that oxidized cellulose undergoes rapid decarboxylation, going to completion after 6 hours boiling in 12% HCl, this frequently being used for determination of carboxyl groups in uronic acids.

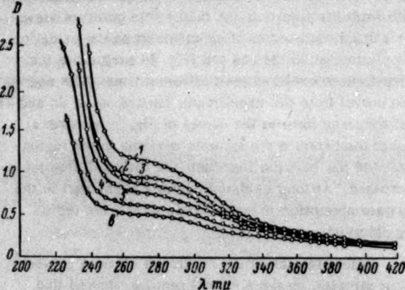


Fig. 4. Absorption spectra of cellulose films, oxidized at 44°, after treating samples with water for 24 hours and drying. Reaction time (in minutes): 1) 180, 2) 238, 3) 113, 4) 418, 5) 26, 6) 8.

An increase in the oxidation temperature can favor an increase in the intra- and intermolecular interaction of carboxyl and hydroxyl groups. Kaverzneva [17] has pointed out that ester and lactone groups are formed on oxidation of cellulose. Besides the chemical method, the lactone group can also be detected by the spectroscopic method [28].

DISCUSSION OF RESULTS

The reaction, which proceeds with the formation of an intermediate product, can be represented by the following scheme: $A \xrightarrow{k_1} B \xrightarrow{k_2} C$. The simplest case of a stepwise reaction was considered by Radovskii [22].

His equations enable us to explain the mechanism observed by us in the oxidation of cellulose by NO_2. The initial product in our case is cellulose: the intermediate—cellulose nitrite, and the end product—monocarboxycellulose. Figure 5 gives curves of change of nitrite content (Curve 1) and carboxyl (Curve 2) with time of oxidation at 31°. As is seen from the graph, the variation of nitrite content with time has all the characteristics of a curve of variation of content of an intermediate product B in a stepwise reaction of the type $A \rightarrow B \rightarrow C$. The accumulation of carboxyl groups in this case is analogous to the accumulation of the end product C. Stepukhovich and Bakhareva [23], in an analysis of the kinetics of stepwise reactions, established that the time of maximum accumulation of intermediate product coincides with the time corresponding to the point of inflection on the curve of accumulation of end product only in the case where the transformations of A to B and of B to C are of the same order. Hence in our case we can assume that the two consecutive reactions are reactions of the same order. Curve 1 of Fig. 5, in fact, passes through a maximum corresponding to the time of the point of inflection that is observed in Curve 2 for the formation of the end product; Curve 2 (Fig. 5) is characterized by an initial rate increase, which also should occur in a stepwise reaction. Note that the similar S-shaped form of the curve of carboxyl group content also agrees with the data [24, 25]. The curve in Fig. 6 shows the variation of rate of formation of carboxyl groups with time.

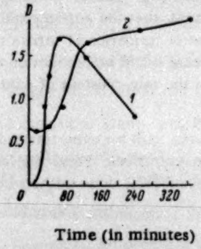


Fig. 5. Change in quantity of nitrite (1) and content of carboxyl groups (2), with time of oxidation at 31°, from absorption spectra data.

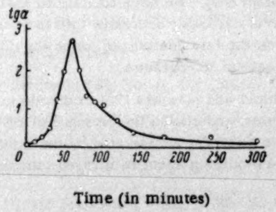


Fig. 6. Change in the relative rate of formation of carboxyl groups with time of oxidation of cellulose by nitrogen peroxide at 31°.

The described relationships of the change of nitrite and carboxyl group contents allow the assumption to be made that the formation of monocarboxycellulose in our experiments proceeds through the formation of cellulose nitrite. Our experimental data and the conclusions drawn from them are in good agreement with the data of a number of other authors, which show that the oxidation of low-molecular alcohols by nitrogen peroxide proceeds through the formation of nitrites [30].

Our data provide a ready explanation also for the acceleration of the reaction on introduction of HNO_3, observed by McGee et al. [11]. Nitric acid reacts with NO_2, forming HNO_2 which esterifies the cellulose simultaneously with the HNO_3 and, by reacting with N_2O_3, regenerates NO_2. From the experiments of Pigman [14] and of Zverev [3], it can be concluded that under conditions which bring about the formation of HNO_2, the reaction will be accelerated. However in their papers the mechanism of the action of HNO_2 is not made clear. It should be particularly noted that with the action of HNO_3, oxidation is considerably accelerated by the addition of $NaNO_2$, which evolves HNO_2, and that on addition of urea, which combines with HNO_2, the reaction is strongly retarded. In all these cases an excess of water retards the reaction and an increase in the $NaNO_2$ content accelerates it. Excess water hinders the formation of cellulose nitrite or assists its hydrolysis.

Let us now turn to Fig. 3 which shows the variation of nitrite content with time of oxidation at different temperatures. On raising the temperature the magnitude of the maximum decreases but the time required for its attainment increases. This implies that in conformity with the analysis of the characteristics of stepwise reactions, at high temperatures the ratio of the rate constant of formation of nitrite to the rate constant of formation of carboxyls decreases.

$$\left(\frac{k_1}{k_2}\right)_{25^\circ} > \left(\frac{k_1}{k_2}\right)_{31^\circ} > \left(\frac{k_1}{k_2}\right)_{44^\circ}$$

The time for the attainment of the maximum nitrite content at 25° is 45 minutes, at 31°, 70 minutes and at 44°, 180 minutes. The quantities of nitrite in the maxima at 25, 31 and 44° are in the ratio 3 : 1.95 : 1.55. It would be interesting to examine how the decrease in the ratio $\frac{k_1}{k_2}$ at high temperatures is related to the change in the rate constants of formation of nitrite and carboxyls in these circumstances.

The curves of Fig. 3 also have another characteristic feature. On increasing the temperature the development of an induction period in the formation of nitrite appears. Possibily at high temperatures the stepwise reaction is complicated by the formation of new intermediate products, prior to the nitrite.

By making use of Fig. 2 we found, by a graphical method, the apparent initial rate of formation of nitrite $\frac{d(x-y)}{dt}$ at different temperatures; this value decreases with increasing temperature. At the same time there is a decrease in the content of the dimer N_2O_4 with increasing temperature as a result of dissociation. Hence it can be assumed that the active agent in the oxidation of cellulose is the dimer N_2O_4. This is not in agreement with Nevell's conclusion, which he drew by analogy with the action of nitric acid, that the active oxidizing agent is the monomer NO_2. We have established that the ratio of the rate constant of formation of nitrite to that of formation of carboxyls decreases with increasing temperature. This decrease could be brought about both by a decrease in the rate constant of formation of nitrite and by an increase in the rate constant of oxidation of nitrite with increase of temperature.

Schmid and Maschka [26] oxidized cyclohexanone and tetrahydrofuran with nitrogen tetroxide at different temperatures, and also in the presence of HNO_3 and HNO_2 at different concentrations. From the fact that the reaction is markedly accelerated by the simultaneous presence of HNO_3 and HNO_2, these authors concluded that the active oxidizing agent is nitrogen tetroxide.

SUMMARY

1. The cellulose nitrite content of the product previously obtained by us by the oxidation of cellulose with nitrogen peroxide has been studied spectroscopically.

It is shown that the quantity of nitrite passes through a maximum with time of oxidation. The maximum quantity of nitrite corresponds to the maximum rate of accumulation of carboxyl groups.

2. An investigation of the variation of the nature of the course of the reaction with temperature has been carried out. With increasing temperature the content of carboxyl groups decreases and also the quantity of nitrite. The maximum in the nitrite-content curve shifts with increasing temperature toward long reaction times and at 65° it no longer appears. This confirms that cellulose nitrite, detected by us, is an intermediate product in the oxidation of cellulose by nitrogen peroxide.

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Received January 14, 1956

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*In Russian.

**Original Russian pagination. See C. B. Translation.

SYNTHESIS OF HETEROORGANIC COMPOUNDS OF THE ALIPHATIC SERIES BY THE DIAZO METHOD

VIII. SYNTHESIS OF COMPOUNDS OF GROUP V ELEMENTS. ORGANOPHOSPHORUS COMPOUNDS. EXPERIMENTS ON THE SYNTHESIS OF DI- AND TRIHALOALKYLPHOSPHINES AND SOME REACTIONS OF CHLOROALKYL DERIVATIVES OF PHOSPHORUS

V. A. Ginsburg and A. Ia. Iakubovich

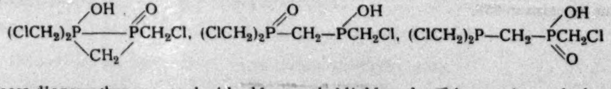
In attempts to extend our diazo method of synthesizing organophosphorus compounds of the aliphatic series [1] to the preparation of secondary and tertiary alkylphosphines by the scheme

$$RCHClPCl_2 \xrightarrow{RCHN_2} (RCHCl)_2PCl \xrightarrow{RCHN_2} (RCHCl)_3P$$

it was established that chloromethyldichlorophosphine and α-chloroethyldichlorophosphine react with diazomethane but under the conditions studied the expected di- and tri-(chloroalkyl)-phosphines were not formed. Instead of them we obtained organophosphorus compounds with a complex structure and a series of properties similar to those of the solid by-products formed by reacting aliphatic diazo compounds with phosphorus trichloride and tribromide. Apparently, the formation of this type of substance was also observed by Plets [2] who had tried unsuccessfully before us to prepare alkylphosphines by reacting diazomethane with phosphorus trichloride.

Chloromethyldichlorophosphine reacted with diazomethane in an ether solution to give a homogeneous, amorphous precipitate that did not distill or recrystallize and did not form any crystallizable derivatives. This made it difficult to isolate it in an analytically pure form. The data from elementary analysis of a series of preparations obtained in various experiments and the value of the molecular weight (found cryoscopically and as the gram-equivalent of a monobasic acid when the substance was titrated with sodium hydroxide in the presence of phenolphthalein) indicated the following empirical composition for the substance: $C_4H_9P_2Cl_3O_2$.

In order to determine the structure of the compound being examined the substance was decomposed with phosphorus pentachloride and also chlorinated with elementary chlorine. In the first case special treatment of the reaction products gave tri-(trichloromethyl)-phosphorus dichloride $(CCl_3)_3PCl_2$ and di-(chloromethyl)-phosphinic and phosphoric acids (in the form of aniline salts). The results obtained indicated that the compound being investigated has one of the following possible formulas, which include groups of atoms that were established experimentally $(\equiv C)_3P$, $(\equiv C)_2P$ and $(\equiv C)-P$.



$$(ClCH_2)_2\overset{OH}{P}-\overset{O}{P}CH_2Cl \text{ (bridged by } CH_2), \quad (ClCH_2)_2\overset{O}{P}-CH_2-\overset{OH}{P}CH_2Cl, \quad (ClCH_2)_2P-CH_2-\underset{O}{\overset{OH}{P}}CH_2Cl$$

In any case diazomethane reacted with chloromethyldichlorophosphine to give undoubtedly new phosphorus-carbon bonds and new chloromethyl groups, connected to phosphorus.

The formation of diphosphorus derivatives containing phosphorus atoms connected by a methylene group, may occur in this reaction either as a result of two phosphorus-containing molecules being connected by a methylene radical, formed during the decomposition of diazomethane, or due to alkylation of the chloromethylphosphine derivative by another molecule, containing trivalent phosphorus, for example by the scheme

$$(ClCH_2)_2PCl + ClCH_2PCl_2 \longrightarrow (ClCH_2)_2PCl_2{-}CH_2PCl_2$$

The occurrence of the latter reactions depends on the lability of the chlorine in the chloromethyl group, connected to phosphorus. To get an idea of the probability of such reactions occurring, we studied the reaction of the diethyl ester of chloromethylphosphinic acid with triethyl phosphite. It was found that the diethyl ester of chloromethylphosphinic acid reacted with triethyl phosphite only under drastic conditions and, in accordance with A. E. Arbuzev's scheme, ethyl chloride and the tetraethyl ester of methylenediphosphinic acid were formed. In addition to these substances considerable amounts of the diethyl ester of ethylphosphinic acid were always present in the reaction products and apparently were formed as a result of the side reaction of triethyl phosphite "isomerization" under the effect of ethyl chloride.

$$P(OC_2H_5)_3 + ClCH_2PO(OC_2H_5)_2 \longrightarrow (C_2H_5O)_2P(O)CH_2PO(OC_2H_5)_2 + C_2H_5Cl$$

$$P(OC_2H_5)_3 \xrightarrow{C_2H_5Cl} C_2H_5PO(OC_2H_5)_2$$

In contrast to the ester of chloromethylphosphinic acid, the diethyl ester of dichloromethylphosphinic acid did not undergo a similar reaction. The lability of a chlorine atom in a carbon chain in a position β to phosphorus was evaluated in a similar reaction, using the diethyl ester of β-chloroethylphosphinic acid and triethyl phosphite as examples, for a qualitative comparison. In this case the reaction, which gave the tetraethyl ester of ethylenediphosphinic acid, proceeded somewhat more readily and less by-product—the diethyl ester of ethylphosphinic acid—was formed.

$$P(OC_2H_5)_3 + ClCH_2CH_2PO(OC_2H_5)_2 \longrightarrow (C_2H_5O)_2P(O)CH_2CH_2PO(OC_2H_5)_2$$

Consequently, the chlorine atom was not very labile in α- and β-haloalkyl derivatives of pentavalent phosphorus (in acid esters) and drastic conditions were required for the formation of diphosphorus derivatives. The lability of the chlorine atom remained the same in the alkylation of phosphorus on going to chloromethyl derivatives of silanes, such as trialkoxychloromethylsilane and even quaternary chloromethyltrimethylsilane, with a less electronegative central atom, silicon. These silanes are quite similar to the previously unknown chloromethyldialkoxy- and chloromethyldialkylphosphines, in which the lability of the chlorine atom should be higher than in the derivatives of pentavalent phosphorus due to the smaller electrophilicity of P^{III}. In fact, chloromethyltrimethylsilane and chloromethyltriethoxysilane react more readily with triethyl phosphite than do chloromethylphosphine derivatives but this reaction, nevertheless, proceeds more readily at about 150° to form silylmethyl phosphine compounds that have not been described previously.

$$P(OC_2H_5)_3 + ClCH_2Si(CH_3)_3 \longrightarrow (C_2H_5O)_2P(O)CH_2Si(CH_3)_3$$

$$P(OC_2H_5)_3 + ClCH_2Si(OC_2H_5)_3 \longrightarrow (C_2H_5O)_2P(O)CH_2Si(OC_2H_5)_3$$

Thus, the formation of diphosphorus derivatives, containing the $P{-}CH_2{-}P$ group of atoms, by a reaction of diazomethane with chloromethyldichlorophosphine (under mild conditions) similar to the formation of phosphonium compounds, is improbable as is shown by the qualitative characteristics given above for the lability of chlorine in a chloromethyl group at a phosphorus atom in the alkylation of trivalent phosphorus compounds and also because of the lower basicity of the phosphorus atom in chloromethylchlorophosphines.

In characterizing tri-(trichloromethyl)-phosphorus dichloride, which we isolated by treating the reaction product of chloromethyldichlorophosphine and diazomethane described above with phosphorus pentachloride, we found that some of its properties are of general interest. This substance was also prepared by heating tri-(chloromethyl)-phosphorus oxide with phosphorus pentachloride.

$$(ClCH_2)_3PO \xrightarrow{PCl_5} (CCl_3)_3PCl_2$$

These observations indicate the particularly ready conversion of chloromethyl groups, connected to phosphorus, into trichloromethyl groups, as we had noted previously [3]. Tri-(trichloromethyl)-phosphorus dichloride is extremely stable to hydrolysis and when treated with boiling water it loses only one of the chlorine atoms connected to the phosphorus.

$$(CCl_3)_5PCl_2 \xrightarrow{H_2O} (CCl_3)_3P(OH)Cl$$

When treated with aniline the tri-(trichloromethyl)-phosphorus hydroxychloride thus obtained lost its acid halide chlorine and was converted to tri-(trichloromethyl)-phosphorus oxide.

$$(CCl_3)_3P(OH)Cl \xrightarrow{C_6H_5NH_2} C_6H_5NH_2 \cdot HCl + (CCl_3)_3PO$$

It seemed interesting to determine whether the stability of the P–Cl bond to hydrolysis we observed in trichloromethylphosphine compounds was maintained in the series of trivalent phosphorus compounds. For this we investigated trichloromethyldichlorophosphine, prepared by reducing trichloromethylphosphorus tetrachloride with yellow phosphorus in the presence of catalytic amounts of phosphorus triiodide.

$$CCl_3PCl_4 \xrightarrow[PI_3]{P} CCl_3PCl_2$$

It was found that when treated with water, trichloromethyldichlorophosphine (low-melting crystals, which were oxidized when heated in air to trichloromethylphosphinyl dichloride) was readily hydrolyzed and in addition to breaking of the P–Cl bond, hydrolytic cleavage of the C–P bond of the molecule occurred and gave phosphorus acid and chloroform. Thus, here the bond between the trichloromethyl group and trivalent phosphorus was found to have a tendency for haloform decomposition to an even greater extent than in the ester of trichloromethylphosphinic acid [4]. Hasseldine et al. [5] noted a similar readiness for hydrolysis of the CF_3–E bond in a series of P, As, Se and S compounds.

EXPERIMENTAL

1. Reaction of diazomethane with chloromethyldichlorophosphine. Preparation of the compound $C_4H_9P_2Cl_3O_2$. With vigorous stirring and cooling to -60°, a solution of 10 g of diazomethane in 300 ml of ether (dried over solid potassium hydroxide) was added dropwise to a solution of 20 g of chloromethyldichlorophosphine in 50 ml of dry ether. The reaction began immediately and was accompanied by the quantitative evolution of nitrogen (about 5 liters) and the formation of a white, curdy precipitate. As soon as the diazomethane decomposition slowed down and the reaction solution acquired a slowly disappearing yellow color, the temperature of the reaction mixture was raised to room temperature and the precipitate filtered off and washed carefully with dry ether. Evaporation of the ether in vacuum yielded 12.5 g of a substance which was readily soluble in water. Evaporation of the water in vacuum gave a hygroscopic glassy mass. Different samples of the substance were analyzed before and after hydrolysis and this gave values which agreed closely and from these, average values from the analysis data of five different samples were obtained.

Found %: C 18.85; H 3.24; Cl_{total}. 41.32; P_{total}. 23.97; P^{III}[*] 12.00. M (in acetic acid and acetophenone) 260; g-equiv. (using phenolphthalein) 256. $C_4H_9P_2Cl_3O_2$. Calculated %: C 18.6; H 3.5; Cl_{total}. 41.3; P_{total}. 24.0; P^{III} (for 1 atom) 12.00. M 257.5; g-equiv. for a monobasic acid 257.5.

The filtrate, remaining after removal of the precipitate, was evaporated in vacuum. There remained 8 g of a viscous, tar-like liquid, which decomposed during distillation.

2. Reaction of $C_4H_9P_2Cl_3O_2$ with phosphorus pentachloride. Preparation of tri-(trichloromethyl)-phosphorus dichloride. 5 g of the substance was heated for 90 minutes with 60 g of PCl_5 on a boiling water bath until it dissolved completely and then the reaction mixture was cooled (on cooling, the mixture crystallized) and sulfur dioxide passed into it. During this treatment the solid mass became liquid. The $POCl_3$ and $SOCl_2$ formed were carefully distilled off in vacuum at 30°. The crystals deposited were separated (2.5 g) to leave the filtrate as a thick, brown liquid (7.0 g). After recrystallization from petroleum ether, the crystals formed fine, colorless prisms with m.p. 190° (with decomp.), which contained hydrolyzable chlorine.

Found %: Cl[**] $_{hydr.}$ 15.58. M 443. $(CCl_3)_3PCl_2$. Calculated %: $Cl_{hydr.}$ 15.52. M 457.5.

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[*] A sample of the order of 0.2 g in 50 ml of 5% aqueous $NaHCO_3$ solution and 50 ml of 0.1 N I_2 was kept in the dark for 4 hours. Then the sample was acidified with 40 ml of 20% H_2SO_4 and the excess I_2 titrated with 0.1 N $Na_2S_2O_3$.

[**] A sample was dissolved in 10 ml of benzene and kept for 24 hours with 5 ml of aniline. The solution was diluted with water and the chlorine determined argentometrically.

3. Preparation of tri-(trichloromethyl)-phosphorus hydroxychloride. 1 g of tri-(trichloromethyl)-phosphorus dichloride was boiled for 30 minutes with 10 ml of water, after which the filtrate was sucked off and the crystals dried in vacuum and recrystallized from petroleum ether. We obtained 0.8 g of a substance with m.p. 203° (with decomp.). Further boiling of the substance with water or aqueous alkali did not produce ionic chlorine.

Found %: C 8.09, 7.91; H 1.01, 0.72; $H_{act.}$ 0.219, 0.274; Cl_{total}. 80.70, 81.10. M 432. $(CCl_3)_3P(OH)Cl$. Calculated %: C 8.20; H 0.228; $H_{act.}$ 0.22; Cl 80.87. M 439.

4. Preparation of tri-(trichloromethyl)-phosphorus oxide. 2 g of $(CCl_3)_3P(OH)Cl$ was dissolved in 60 ml of benzene and 3.0 g of aniline added to the solution. After 1 day 0.58 g of aniline hydrochloride had precipitated. After being washed with 5% aqueous hydrochloric acid, the benzene solution was dried over sodium sulfate; the benzene was removed in vacuum. We obtained 1.2 g of tri-(trichloromethyl)-phosphorus oxide, which melted at +55° after recrystallization from methanol (with cooling to -70°). It was insoluble in water and aqueous alkali.

Found %: Cl 79.91, 79.30. M 412. $(CCl_3)_3PO$. Calculated %: Cl 79.38. M 402.5.

5. Hydrolysis of the liquid products formed during phosphorus pentachloride treatment of the compound $C_4H_9P_2Cl_3O_2$. The liquid filtrate remaining after separation of tri-(trichloromethyl)-phosphorus dichloride (see Experiment 2) was hydrolyzed and the mixture of acids formed resolved via aniline salts. 4.5 g of the liquid was treated with 30 ml of water for 3 days at room temperature. When the substance had dissolved, the water was removed in vacuum with a bath temperature of 30°. The residue was dissolved in 200 ml of amyl alcohol and 5 ml of aniline added. The precipitate of aniline salts was filtered off and recrystallized several times. We isolated 4.5 g of plate-like crystals with m.p. 180° and 0.5 g of thin needles, which were readily soluble in alcohol and reprecipitated from it by the addition of 50 volumes of benzene (m.p. 185–190° with decomp.).

Found %: C 37.84, 37.93; H 4.91, 3.99; Cl 27.08, 27.81; N 6.34, 6.07. $(ClCH_2)_2POOH \cdot C_6H_5NH_2$. Calculated %: C 37.50; H 4.70; Cl 27.37; N 5.45.

The plate-like crystals were aniline phosphate.

Found %: C 49.39, 48.87; H 6.43, 6.33; N 10.07, 9.88. $H_3PO_4 \cdot 2C_6H_5NH_2$. Calculated %: C 50.70; H 5.98; N 9.85.

6. Action of chlorine on the compound $C_4H_9P_2Cl_3O_2$. 5 ml of CCl_4 was poured onto 5 g of the substance, which was chlorinated with elementary chlorine at 50° for 3 days. The bulk of the substance was converted into a product which was viscous when heated and friable in the cold. 4 g of the substance obtained was dissolved in 10 ml of water and the excess water removed in vacuum at room temperature. The sirupy residue was dissolved in amyl alcohol; the solution was then treated with 5 ml of aniline. The precipitated aniline salt (2 g) was separated and recrystallized from alcohol: the fine needles with m.p. 182–185° (with decomp.) were the aniline salt of chloromethylphosphinic acid. A mixed melting point of this substance and an authentic sample of the salt named was not depressed.

Found %: C 37.07, 37.13; H 5.53, 5.45; Cl 15.05, 15.33; N 7.48. $ClCH_2PO(OH)_2 \cdot C_6H_5NH_2$. Calculated %: C 37.60; H 4.03; Cl 15.90; N 6.26.

7. Action of phosphorus pentachloride on tri-(chloromethyl)-phosphorus oxide; preparation of tri-(trichlormethyl)-phosphorus hydroxychloride. 1 g of tri-(chloromethyl)-phosphorus oxide was mixed with 3 ml of phosphorus trichloride and 12 g of phosphorus pentachloride. The mixture was boiled gently for 30 minutes under reflux. Then the PCl_3 and $POCl_3$ were distilled off in vacuum, the residue treated with sulfur dioxide at room temperature and the filtrate sucked off. After treating the precipitate with hot water, we obtained 0.8 g of fine crystals, which separated as colorless needles with m.p. 200–202° (with decomp.) after two recrystallizations from benzine. The product did not contain chlorine, which was hydrolyzable under normal conditions. A mixed melting point with tri-(chloromethyl)-phosphorus hydroxychloride, obtained as described above, was not depressed.

Found %: Cl 81.16; P 7.78, 7.68. $(CCl_3)_3P(OH)Cl$. Calculated %: Cl 80.87; P 7.05.

8. Reaction of the diethyl ester of chloromethylphosphinic acid with triethyl phosphite. A mixture of 26.2 g of triethyl phosphite and 29.2 g of the diethyl ester of chloromethylphosphinic acid was heated for 8 hours at 185–190° in 3 ampules. Several distillations yielded the fractions: 1st b.p. 11.5–12.5°, 6.4 g; 2nd b.p. 70–

–90° (20 mm), 6.5 g; 3rd b.p. 90–95° (20 mm), 9.2 g; 4th b.p. 80–90° (4 mm), 4.1 g; 5th b.p. 90–95° (4 mm), 16.3 g; 6th b.p. 153–154° (3 mm), 12.1 g; total 54.6 g.

The boiling point and the molecular weight of 63.5 of the 1st fraction identified it as ethyl chloride. The 3rd fraction did not contain chlorine, had d^{20}_{20} 1.031, $n^{20}D$ 1.4155, and was the diethyl ester of ethylphosphinic acid.

Found %: C 43.60; H 9.27; OC_2H_5 53.75. M 159 (in benzene). $C_2H_5PO(OC_2H_5)_2$. Calculated %: C 43.40; H 9.05; OC_2H_5 54.2. M 166.

The 5th fraction was the starting diethyl ester of chloromethylphosphinic acid.

Found %: OC_2H_5 47.54. M 182 (in benzene). $ClCH_2PO(OC_2H_5)_2$. Calculated %: OC_2H_5 48.3. M 186.5.

The 6th fraction was a thick liquid, which did not contain chlorine, had d^{20}_{20} 1.167, $n^{20}D$ 1.4415 and was the tetraethyl ester of methylenediphosphinic acid.

Found %: 37.25, 37.34; H 6.75, 6.51; OC_2H_5 61.87, 61.99. M 292 (in benzene). $(C_2H_5O)_2P(O)CH_2PO(OC_2H_5)_2$. Calculated %: C 37.5; H 7.65; OC_2H_5 62.5. M 288.

Fractions 2 and 4 were intermediate.

Hydrolysis of tetraethyl ester of methylenediphosphinic acid. 1 g of material from the 6th fraction was boiled for 2 hours with 10 ml of 15% hydrochloric acid. Evaporation in vacuum and recrystallization from acetic acid yielded 0.2 g of methylenediphosphinic acid crystals with m.p. 199–200° [6].

9. *Reaction of diethyl ester of β-chloroethylphosphinic acid with triethyl phosphite.* A mixture of 12 g of the diethyl ester of β-chloroethylphosphinic acid and 28 g of triethyl phosphite was heated at 185–190° for 8 hours in sealed tubes. The reaction products, which contained ethyl chloride and the diethyl ester of ethylphosphinic acid, yielded a fraction with b.p. 170–175° (3 mm), 5.5 g, d^{20}_{20} 1.080, $n^{20}D$ 1.4425, which was the tetraethyl ester of ethylenediphosphinic acid.

Found %: OC_2H_5 58.75. M 308 (in benzene). $(C_2H_5O)_2P(O)CH_2CH_2PO(OC_2H_5)_2$. Calculated %: OC_2H_5 59.5. M 302.

10. *Reaction of chloromethyltrimethylsilane with triethyl phosphite.* A mixture of 12.3 g of triethyl phosphite and 10 g of chloromethyltrimethylsilane was heated at 170° for six hours in two ampules. We isolated 5.9 g of the diethyl ester of trimethylsilylmethylphosphinic acid with b.p. 79–80° (3 mm), d^{20}_{20} 0.9878, $n^{20}D$ 1.4280.

Found %: OC_2H_5 39.66, 39.46; P 13.11, 13.51; Si 12.37, 12.21. M 212.5 (in benzene). $(CH_3)_3SiCH_2PO(OC_2H_5)_2$. Calculated %: OC_2H_5 40.2; P 13.85; Si 12.5. M 224.

11. *Reaction of triethyl phosphite with chloromethyltriethoxysilane.* 10.25 g of chloromethyltriethoxysilane with b.p. 72–74° (12 mm) (prepared from chloromethyltrichlorosilane and alcohol in the presence of diethylaniline) and 8.0 g of triethyl phosphite were heated in an ampule as described in experiment 10. We isolated 15.5 g of the diethyl ester of triethoxysilylmethylphosphinic acid with b.p. 133–135° (3 mm), d^{20}_{20} 0.995.

Found %: OC_2H_5 69.97, 70.40; P 10.25, 9.85; Si 8.11, 7.95. M 299 (in benzene). $(C_2H_5O)_3SiCH_2PO(OC_2H_5)_2$. Calculated %: OC_2H_5 71.5; P 9.9; Si 8.9. M 314.

12. *Reduction of trichloromethylphosphorus tetrachloride to trichloromethyldichlorophosphine.* To a suspension of 12 g of trichloromethylphosphorus tetrachloride in 40 ml of dry carbon tetrachloride was added 0.5 g of phosphorus triiodide and with vigorous mixing in an atmosphere of nitrogen, a solution of 1.1 g of yellow phosphorus in 10 ml of carbon disulfide was added. A homogeneous liquid was quickly formed and the solvent was removed from this in vacuum; the residue was distilled. A second distillation yielded 5.5 g of colorless, hygroscopic crystals, which were readily oxidized in air and had b.p. 82–83° (7 mm) (with decomp.) and m.p. about 50–52°.

Found %: P 11.73, 11.27; Cl 81.85, 82.13 (combustion). M 238 (in benzene). CCl_3PCl_2. Calculated %: P 12.1; Cl 83.5. M 256.

0.5 g of the substance was left for 1 hour on a watch glass in a desiccator containing dry air. The crystals formed were treated with hot water. Removal of the water in vacuum gave 0.3 g of crystals with m.p. 77–79° (from CCl_4). A mixed melting point with authentic trichloromethylchlorophosphinic acid was not depressed.

1 g of the substance in 3 ml of dry ether was added dropwise (in nitrogen) to 10 ml of water, from which the oxygen had first been expelled by boiling in an atmosphere of nitrogen. After removing the solvent in vacuum, we obtained 0.3 g of a sirupy liquid. The substance gave calomel when heated with a solution of mercuric chloride. After boiling with nitric acid, the substance gave a positive molybdate test for phosphoric acid. Chloroform (isonitrile reaction with aniline) was present in the aqueous ether distillate.

SUMMARY

1. Using the reaction of chloromethyldichlorophosphine with diazomethane as an example, it was shown that this reaction did not give di- and tri-(chloromethyl)-phosphines.

Chlorination of the product obtained from the above reaction gave tri-(trichloromethyl)-phosphorus dichloride and di-(chloromethyl)-phosphinic and phosphoric acids (in the form of aniline salts). The scheme for the formation, and the structures of these compounds are discussed.

2. It was shown that the esters of chloromethyl- and β-chloroethylphosphinic acids undergo an Arbuzov reaction at high temperatures and form esters of methylene- and ethylenediphosphinic acids, respectively, with triethyl phosphite.

3. Chlorination of tri-(chloromethyl)-phosphorus oxide with phosphorus pentachloride gave tri-(trichloromethyl)-phosphorus dichloride which was hydrolyzed to tri-(trichloromethyl)-phosphorus hydroxychloride. This substance was stable to hydrolysis; when treated with aniline it was converted to tri-(trichloromethyl)-phosphorus oxide.

4. Trichloromethylphosphorus tetrachloride was reduced with yellow phosphorus to give trichloromethyldichlorophosphine, which split out chloroform when treated with water.

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Received January 25, 1957

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*Original Russian pagination. See C. B. Translation.

IODO DERIVATIVES OF METHYLPHOSPHINE

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Iodides of organic acids of phosphorus have hitherto been represented only by phenylphosphine diiodide, obtained in the form of the hydroiodide by Michaelis [1] and Lecoq [2] by reaction of phenylphosphine dichloride with gaseous hydrogen iodide. It was found that alkylphosphine iodides can be prepared by reaction of acid chlorides of alkylphosphonic and alkylphosphonous acids with hydrogen iodide. This is illustrated in the present work by the preparation of iodo derivatives of methylphosphine. Treatment of methylphosphonic dichloride (in chloroform) with gaseous hydrogen iodide at room temperature gives dark-red crystals of an iodo derivative with m.p. 156°, whose composition corresponds to the formula CH_3PI_4. The compound is easily soluble in water with copious release of iodine and formation of methylphosphonic acid.

Phosphorus pentaiodide is known to be extremely unstable and cannot be isolated. Moreover, according to Fursman and Lipkin [3], some compounds of trivalent phosphorus, notably triphenyl phosphite, form a series of iodo derivatives with covalently bound iodine, including $(C_6H_5O)_3PI_4$ and $(C_6H_5O)_3PI_9$. We treated our prepared methylphosphorus tetraiodide with excess of dry sodium ethoxide with the aim of confirming its structure as a true compound of pentavalent phosphorus. Under conditions excluding oxidation this gave the diethyl ester of methylphosphonic acid. To a certain extent, this result rules out the possibility that this substance is the complex $CH_3PI_2 \cdot I_2$.

Apart from methylphosphorus tetraiodide, the reaction mixture gave (after distillation of the solvent) a resinous mass which evidently consisted of products of partial hydrolysis of acid chlorides present in the reaction medium. Treatment with water converts this mass into methylphosphonic acid. In a general way the process can be represented by the equation

$$3CH_3POCl_2 + 8HI \longrightarrow 2CH_3PI_4 + CH_3PO(OH)_2 + 6HCl$$

Reaction of hydrogen iodide with methyldichlorophosphine under similar conditions gives a crystalline product with m.p. 85–87°, outwardly resembling iodine and quite different in properties from the iodide described above. Its composition corresponds to the hydroiodide of methylphosphorus diiodide. Hardly any iodine is released when the compound dissolves in water, and the characteristic odor of phosphine is detected. It is evident that in reaction with hydrogen iodide aliphatic phosphonic dichlorides behave like aromatic compounds [1,2]:

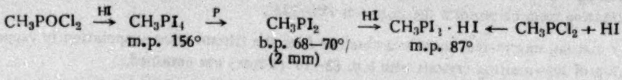
$$CH_3PCl_2 \xrightarrow{3HI} CH_3PI_2 \cdot HI + 2HCl$$

Experiments on the reduction of methylphosphorus tetraiodide were undertaken with the objective of preparing free methylphosphine diiodide. The reduction was found to proceed with facility under the action of yellow phosphorus in a medium of carbon disulfide. Methylphosphine diiodide forms low-melting, cherry-red crystals; b.p. 68–70° (2 mm). It is hygroscopic; on treatment with aqueous alkali it releases methylphosphine. Fractional crystallization of the reaction mass gave in addition diphosphorus tetraiodide, possibly according to the equation:

$$2CH_3PI_4 + 2P \longrightarrow 2CH_3PI_2 + P_2I_4$$

Reaction of the resulting methylphosphorus diiodide with hydrogen iodide gave the hydroiodide with m.p. 85–86°, identical with the product of reaction of methylphosphorus dichloride with hydrogen iodide.

All of the investigated transformations in the series of methylphosphine iodides are represented by the scheme



$$\underset{}{CH_3POCl_2} \xrightarrow{HI} \underset{\text{m.p. }156°}{CH_3PI_4} \xrightarrow{P} \underset{\substack{\text{b.p. }68\text{–}70°/\\ (2\text{ mm})}}{CH_3PI_2} \xrightarrow{HI} \underset{\text{m.p. }87°}{CH_3PI_2 \cdot HI} \longleftarrow CH_3PCl_2 + HI$$

During the course of this investigation papers were published by Walsh and co-workers that described the reduction of higher alkylphosphorus tetrachlorides to alkylphosphorus dichlorides under the action of yellow phosphorus [4,5]. These authors refer to the catalytic role of iodine in this reduction (in its absence the reaction reportedly does not take place). We found that iodides of phosphorus are readily reduced by yellow phosphorus in the absence of any catalyst. It was shown in particular that under the action of yellow phosphorus, phosphorus triioide is quantitatively transformed into diphosphine tetraiodide. It is not excluded that the iodine is involved in an exchange reaction leading to intermediate formation of alkylphosphine iodides which easily react with yellow phosphorus.

EXPERIMENTAL

1. Interaction of methylphosphonic acid dichloride with hydrogen iodide. Preparation of methylphosphorus tetraiodide. Hydrogen iodide (dried over P_2O_5) was slowly bubbled into a solution of 20 g of methylphosphonic acid dichloride in 50 ml of dry chloroform at room temperature. The temperature in the reaction mixture rose to 45–50°, the solution acquired a red color, and cherry-red crystals were deposited. A total of 68 g of hydrogen iodide was passed through, of which 37 g combined. After 12 hours, the crystals were collected by decantation of the solvent, washed with dry chloroform and dried in vacuo. Yield 38.7 g with m.p. 156°.

Found %: P 6.00, 6.10; I 91.69, 91.94. M 545 ($POCl_3$). CH_3PI_4. Calculated %: P 5.6; I 91.64. M 554.

The yield of methylphosphorus tetraiodide was 97% (on the hydrogen iodide reacted). Further passage of hydrogen iodide led to resinification which complicated the purification of the substance. Removal of the chloroform from the solution left 13 g of viscous, resinous mass which after boiling with water was converted into methylphosphonic acid (9 g).

Hydrolysis of methylphosphorus tetraiodide. 5 g of CH_3PI_4 with m.p. 156° was dissolved in 200 ml of water. The solution was evaporated to dryness on a water bath and dried in a vacuum-desiccator over P_2O_5 to give 0.7 g of hygroscopic crystals with m.p. 99–100°, in agreement with the m.p. of methylphosphonic acid. 0.5 ml of aniline was run into 0.5 g of the acid and 5 ml of alcohol. The precipitated needles of the anilide were recrystallized from alcohol. M.p. 148–150°.

Found %: N 8.11, 8.15. $CH_3PO(OH)_2 \cdot C_6H_5NH_2$. Calculated %: N 7.41.

Reaction of methylphosphorus tetraiodide with dry sodium ethoxide. To a suspension of 10 g of dry, powdered sodium ethoxide in 50 ml of benzene was added 20 g of methylphosphorus tetraiodide with vigorous stirring. The temperature in the reaction mixture rose to +70° and the iodide lost its color. After 30 minutes the solution was filtered from the solid in a nitrogen atmosphere and fractionally distilled to give 1.75 g (35%) of the diethyl ester of methylphosphonic acid with b.p. 90–92° (10 mm), M 148 (in benzene), $d^{20}D$ 1.058, $n^{20}D$ 1.4138.

2. Reaction of methylphosphine dichloride with hydrogen iodide. Preparation of methylphosphine diiodide hydroiodide. Dry hydrogen iodide was bubbled at room temperature into a solution of 11.5 g of methylphosphine dichloride in 40 ml of dry chloroform. A little heat was generated during the reaction and crystals with the appearance of iodine came down. A total of 41.5 g of hydrogen iodide was passed through and 33.5 g reacted. The crystals were filtered off, washed with dry chloroform and dried in a current of carbon dioxide. Yield 28.2 g of substance with m.p. 85–87°. The yield was equivalent to 75% when calculated on the hydrogen iodide.

Found %: P 7.41, 7.31; I 88.50, 88.80. M 405 ($POCl_3$). $CH_3PI_2 \cdot HI$. Calculated %: P 7.25; I 89.0. M 428.

3. Reduction of methylphosphorus tetraiodide with yellow phosphorus. Preparation of methylphosphorus diiodide. 10.7 g of methylphosphorus tetraiodide (m.p. 156°) was added at room temperature to a solution of 0.6 g of yellow phosphorus in 15 ml of dry carbon disulfide. The iodide dissolved on shaking, and crystals of diphosphorus tetraiodide later came down. These were separated at room temperature and a further batch was obtained on freezing the filtrate in carbon dioxide. A total of 8.0 g of P_2I_4 was collected; m.p. 115–122°. After recrystallization from chloroform the m.p. was 123–124°.

3.5 g of a viscous, cherry-red liquid was obtained from the filtrate after evaporation in vacuo. After two distillations, 2.5 g of low-melting crystals with b.p. 68–70° (2 mm) was obtained.

Found %: P 9.60, 9.80; I 84.89, 85.11. M 295 (in benzene). CH_3PI_2. Calculated %: P 10.3; I 85.0. M 300.

Preparation of methylphosphine diiodide hydroiodide. A stream of dry hydrogen iodide was bubbled into a solution of 0.85 g of methylphosphine diiodide in 3 ml of dry chloroform until crystals ceased to come down. The crystals were separated, washed with dry chloroform and dried in vacuo. Yield 0.8 g of the hydroiodide with m.p. 85–86°. A mixture with a specimen prepared from methylphosphine dichloride did not give a depression of melting point.

4. Reduction of phosphorus triiodide with yellow phosphorus to diphosphorustetraiodide. To a solution of 0.3 g of yellow phosphorus in 10 ml of dry carbon disulfide was added 8 g of phosphorus triiodide (m.p. 61°). Orange crystals of P_2I_4 came down from the solution after 30 minutes; m.p. 124°; yield quantitative.

SUMMARY

1. Reaction of hydrogen iodide with chlorides of methylphosphonic and methylphosphonous acids gave the iodides CH_3PI_4 and $CH_3PI_2 \cdot HI$ which had not previously been described.

2. Reduction of methylphosphorus tetraiodide with yellow phosphorus gave methylphosphine diiodide. Under the same conditions phosphorus triiodide is quantitatively converted into diphosphorus tetraiodide.

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Received January 25, 1957

REACTIONS OF MAGNESYLAMINES

IV. ARYLAMIDATION OF AROMATIC ALDEHYDES WITH THE HELP OF ARYLAMINE-N,N-DIMAGNESIUM HALIDES

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In continuation of our work [1] on arylamidation of benzaldehyde with the help of arylamine-N,N-dimagnesium halides* we carried out the present investigation with the objective of extending the reaction to other aromatic aldehydes. In this connection it was necessary to establish the conditions that would considerably increase the yield of reaction products, since in the earlier work the yields of arylamides in the majority of cases did not exceed 15–18%.

Using aniline-N,N-dimagnesium bromide and p-toluidine-N,N-dimagnesium bromide as the amine component and benzaldehyde as the aldehydic component, it was shown that the solvent has an important influence on the yield of arylamides (Table 1). The table indicates that the yield of arylamides increases with the boiling point of the solvent (Experiments 1 to 4). The highest yields were obtained, however, by operating in pyridine and dioxan (Experiments 5 and 6). In the latter case the basic properties of the solvents may have favorably influenced the yield of benzarylamides.

TABLE 1

Preparation No.	Solvent	Yield (in %)	
		$C_6H_5CONHC_6H_5$	$C_6H_5CONHC_6H_4CH_3$-p
1	Ether	17.3	17.1
2	Benzene	19.8	18.8
3	Toluene	25.9	19.9
4	Xylene	40.6	33.6
5	Pyridine	51	48.5
6	Dioxan.	51.5	–

The duration of heating of the reaction mass also influences the yield of arylamides: the best results are obtained by 15-minutes' heating; longer heating leads to resinification.

Later experiments showed that the reaction that we had discovered for arylamidation of aldehydes with the help of dimagnesylamines can be successfully extended to various aromatic aldehydes (Table 2). We see from the data in this table that in the majority of cases arylamides are obtained in 50–90% yields and higher, so that our reaction can be said to stand comparison with the usual methods of preparative chemistry.

Arylamides (I-IX) have not been described in the literature; they are crystalline substances, sparingly soluble in ether, gasoline and chloroform, readily soluble in other organic solvents. The literature [4] reports m.p. 73° for the p-toluidide of p-chlorobenzoic acid (VIII) which is incorrect.

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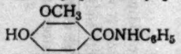
* Arylamine-N,N-dimagnesium halides will be called dimagnesylamines in the further course of this paper.

TABLE 2

Prep. no.	Aldehyde	Ar in ArN (MgBr)$_2$	Reaction product	Yield (%)	Type of crystals	Melting point [2]	Analysis for nitrogen (%)	
							found	calculated
1	p-$CH_3C_6H_4CHO$	C_6H_5	p-$CH_3C_6H_4CONHC_6H_5$	33.5	—	146°	—	—
2	p-BrC_6H_4CHO	the same	p-$BrC_6H_4CONHC_6H_5$	98.55	—	200—201	—	—
3	p-ClC_6H_4CHO	the same	p-$ClC_6H_4CONHC_6H_5$	83.8	—	194—195	—	—
4	p-$(CH_3)_2NC_6H_4CHO$	the same	p-$(CH_3)_2NC_6H_4CONHC_6H_5$	95.0	—	180—182	—	—
5	m-ClC_6H_4CHO	the same	m-$ClC_6H_4CONHC_6H_5$	91.1	—	136—137	—	—
6	p-$CH_3OC_6H_4CHO$	the same	p-$CH_3OC_6H_4CONHC_6H_5$	70.4	—	168—169	—	—
7	m-$CH_3C_6H_4CHO$	the same	m-$CH_3C_6H_4CONHC_6H_5$ (I)	53.3	Plates *	129—130	6.84, 6.73	6.63
8	m-BrC_6H_4CHO	the same	m-$BrC_6H_4CONHC_6H_5$	70	—	146—147.5	—	—
9	p-OH-(m-OCH_3)·C_6H_3CHO	the same	 (II)	53.5	Prisms **	129—131	5.52, 5.68	5.76
10	p-BrC_6H_4CHO	p-ClC_6H_4	p-$BrC_6H_4CONHC_6H_4Cl$-p (III)	69.7	Plates **	217—217.5	4.58, 4.47	4.51
11	the same	p-$CH_3C_6H_4$	p-$BrC_6H_4CONHC_6H_4CH_3$-p	64.4	—	232—233[3]	—	—
12	the same	p-BrC_6H_4	p-$BrC_6H_4CONHC_6H_4Br$-p	67.6	—	222	—	—
13	the same	p-$CH_3OC_6H_4$	p-$BrC_6H_4CONHC_6H_4OCH_3$-p (IV)	52.4	Plates **	222—223	4.50, 4.59	4.57
14	the same	α-$C_{10}H_7$	p-$BrC_6H_4CONHC_{10}H_7$-α (V)	51.5	Plates **	211—212	4.56	4.29
15	the same	β-$C_{10}H_7$	p-$BrC_6H_4CONHC_{10}H_7$-β (VI)	78.5	Needles	218—218.5	4.21, 4.26	4.29
16	p-ClC_6H_4CHO	β-$C_{10}H_7$	p-$ClC_6H_4CONHC_{10}H_7$-β (VII)	92.3	Plates **	206—207	5.06, 5.12	4.97
17	the same	p-$CH_3C_6H_4$	p-$ClC_6H_4CONHC_6H_4CH_3$-p (VIII)	50.5	Plates **	212—213	5.65, 5.54	5.70
18	the same	p-$CH_3OC_6H_4$	p-$ClC_6H_4CONHC_6H_4OCH_3$-p (IX)	53.5	Plates **	208—209	5.37, 5.24	5.35
19	the same	p-ClC_6H_4	p-$ClC_6H_4CONHC_6H_4Cl$-p	75.3	—	207—208	—	—

*Alcohol used as crystallization solvent.

**Acetic acid used for crystallization.

EXPERIMENTAL

Experimental procedure. Ethylmagnesium bromide was prepared from 0.025 mole of ethyl bromide and 0.025 mole of magnesium in 20 ml of ether. Addition was made to it of 0.0125 mole of aromatic amine in 15 ml of ether and the mixture was heated for 10–15 minutes on a water bath. The ether was driven off on a boiling water bath and a solution of 0.025 mole of aldehyde in 20 ml of dry pyridine was added to the residue; the mixture was then boiled for 5 minutes on a sand bath. The organomagnesium complex was decomposed with dilute hydrochloric acid and the reaction mass was twice treated with ether. The ether and the volatile products of reaction were distilled off with steam. The residue in the distillation flask was filtered, dried in the air and recrystallized from a suitable solvent. If a precipitate came down on decomposition of the organomagnesium complex, the precipitate was filtered, treated with steam and worked up as described above. In Experiment 9 (Table 2) the dimagnesylamine was taken in 1 : 1 ratio to the vanillin. The yield of arylamides was calculated on the aromatic amine taken into reaction.

A slightly modified procedure was employed for Experiments 1 to 4, 10 and 11 (Table 2). The ether was driven off from the ethylmagnesium bromide and a solution of the aromatic aldehyde in dry pyridine was added. To the resulting dimagnesylamine was added a pyridine solution of the aldehyde, the reaction mass was heated for 1 hour on the sand bath and decomposed with hydrochloric acid. The product was worked up as in the previous experiments.

The first procedure was found more convenient since less time was consumed both on the performance of the reaction itself and on the isolation of the reaction products. In addition the latter are obtained with higher purity and in satisfactory yields.

Beech's synthesis [5] of aromatic aldehydes. The aromatic aldehydes used in this work were prepared by Beech's method [5] with exception of p-dimethylaminobenzaldehyde and vanillin. His method was slightly modified. First, sodium acetate was not added to the solution of diazo compound, but the calculated quantity of the former was added to the solution of formaldehyde oxime. Secondly, hydrolysis of the oxime of the aldehyde was not performed directly in the reaction medium (as in Beech's procedure) but after its isolation. This leads to a considerable drop in the volume of the reaction mass and to shortening of the time needed for carrying out the experiment. Thirdly, prior to decomposition of the bisulfite compound the reaction mass was heated on a water bath until the dissolved ether had been completely removed. If the ether was not entirely removed, it was difficult to completely decompose the bisulfite compound and the yield of aldehyde was much lower.

SUMMARY

1. The effect of the nature of the solvent on the yield on arylamides of carboxylic acids was studied; it was found that the highest yields of arylamides are obtained when the experiments are performed in pyridine and dioxan.

2. The reaction of arylamidation of aldehydes with the help of dimagnesylamines was successfully extended to various aromatic aldehydes, and the optimum conditions for preparative employment of the reaction were established.

3. A number of previously undescribed arylamides of aromatic acids were prepared and their properties studied.

4. Beech's method of preparation of aromatic aldehydes was improved.

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Perm Institute of Pharmacy

Received January 21, 1957

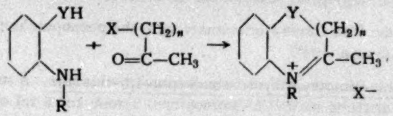
CONDENSATION OF o-AMINOTHIOPHENOLS WITH β-HALOKETONES

SYNTHESIS OF QUATERNARY SALTS IN THE DIHYDROBENZOHEPTA-1,5-THIAZINE SERIES. III

L. K. Mushkalo

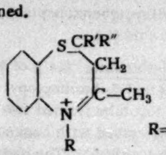
Quaternary salts of the dihydrobenzohepta-1,5-thiazine series are obtained by the usual method of alkylation of the corresponding bases, as well as by the action of mineral acids on derivatives of 5-alkyl- and 5-phenyldihydrobenzohepta-1,5-thiazines [1]. The yield of quaternary salts by this route does not exceed 50% reckoned on the original aminothiols. In the present communication we describe a new method of preparation of quaternary salts of seven-membered heterocycles by condensation of N-alkyl- and N-phenyl-o-aminothiophenols with β-haloketones.

This method is one case of a general method of preparation of quaternary salts of heterocyclic bases. As previously shown [2], condensation of N-alkyl- and N-phenyl-o-aminothiophenols and of N-substituted o-aminophenols with carboxylic acid chlorides gives quaternary salts of benzothiazole (or benzoxazole). If, however, the halogen is subsequently transferred from the carbonyl group to the halocarbonyl component, quaternary salts of six- and seven-membered heterocycles are obtained.



Y = S, O; X = halogen; R = alkyl, aryl; n = 0, 1, 2.

For example, condensation of N-alkyl- and N-aryl-o-aminothiophenols with α-haloketones (n = 1) gives quaternary salts of benzo-1,4-thiazine [2]; with β-haloketones, as we showed, quaternary salts of seven-membered heterocycles are formed.

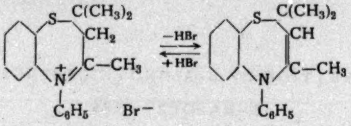


R=CH_3, C_2H_5, C_6H_5; R′and R″=H, CH_3.

This method gives good yields of quaternary salts, and it can be recommended for preparations of quaternary salts of the dihydrobenzohepta-1,5-thiazine series. Condensation of N-alkyl- and N-phenyl-o-aminothiophenols with methyl-β-bromoethyl ketone and its closest homologs proceeds with facility and with considerable evolution of heat. This reaction goes best of all in benzene solution.

Conversion of the quaternary salts to the perchlorates is recommended for their isolation and purification. The perchlorates crystallize easily. The yield of quaternary salts by this method reaches 70–90%.

The free bases can be isolated by treatment of quaternary salts of the dihydrobenzohepta-1,5-thiazine series with an aqueous solution of caustic alkali. Alkali treatment, for example, of an aqueous solution of the phenobromide of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine gives the crystalline base, which with mineral acids again gives the original quaternary salt.



The methyl group in the 4-position of these salts possesses active hydrogen atoms. Our synthesized quaternary salts can accordingly be employed for the synthesis of cyanine dyes [3].

EXPERIMENTAL

Phenobromide of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine. A mixture of 2.1 g of N-phenyl-o-aminothiophenol, 1.8 g of freshly distilled methyl β-bromoisobutyl ketone and 3 ml of benzene was heated on a water bath. The resulting exothermic reaction was completed in a few seconds. The bottom layer, containing the quaternary salt, was separated and a few milliliters of acetone was added. Rubbing with a glass rod caused the quaternary salt to crystallize. The crystals were filtered and washed successively with acetone and alcohol. Yield of phenobromide of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine 3.6 g (70%), m.p. 147°.

Found %: Br 22.10, 22.37. $C_{18}H_{20}SNBr$. Calculated %: Br 22.09.

2,2,4-Trimethyl-5-phenyldihydrobenzohepta-1,5-thiazine. An aqueous solution of 0.6 g of the phenobromide of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine was shaken with aqueous caustic alkali. The liberated base was extracted with ether and dried with solid potassium hydroxide. The base crystallized after the ether had evaporated. Yield 0.2 g of 2,2,4-trimethyl-5-phenyldihydrobenzohepta-1,5-thiazine with m.p. 97°.

Found %: N 4.96, 5.02. $C_{18}H_{19}NS$. Calculated %: N 4.95.

With perchloric acid the base forms a quaternary salt—the phenoperchlorate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine with m.p. 190°.

Methoperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine. A mixture of 5 g of N-methyl-o-aminothiophenol, 6.5 g of freshly distilled methyl β-bromopropyl ketone and 5 ml of benzene was heated on a water bath for 20 minutes. The lower layer of quaternary salt weighed 7.7 g (70%) and was a vitreous mass which did not crystallize. The perchlorate of the quaternary salt was prepared by treating an alcoholic solution of the methobromide of 2,4-dimethyldihydrobenzohepta-1,5-thiazine with perchloric acid. After recrystallization from alcohol, the crystals of methoperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine had m.p. 111° and were identical with the methoperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine prepared from 2,4,5-trimethyldihydrobenzohepta-1,5-thiazine and perchloric acid [1].

Phenoperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine. 2.4 g of N-phenyl-o-aminothiophenol was mixed with 3 ml of benzene and 2 g of freshly distilled methyl β-bromopropyl ketone. An exothermic reaction commenced in a few minutes and the contents of the test tube formed two layers. The lower layer of quaternary salt was separated from the upper benzene layer and washed with benzene and ether. Yield of phenobromide of 2,4-dimethyldihydrobenzohepta-1,5-thiazine 4 g (95%). The quaternary salt is a vitreous mass. The perchlorate was obtained by the action of 30% perchloric acid on an alcoholic solution of the quaternary salt. After recrystallization from alcohol, the phenoperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine had m.p. 198°.

Found %: Cl 9.82, 9.70. $C_{17}H_{18}O_4NSCl$. Calculated %: Cl 9.68.

Phenobromide of 4-methyldihydrobenzohepta-1,5-thiazine. To a solution of 2 g of N-phenyl-o-aminothiophenol in 2 ml of benzene was added 1.5 g of freshly distilled methyl β-bromoethyl ketone. Heat was liberated and the exothermic reaction quickly came to an end. After heating for 10 minutes on a water bath, the lower layer of quaternary salt was separated from the upper benzene layer and washed with benzene and ether. After drying in an extractor over paraffin wax, the quaternary salt was a colorless, vitreous mass which was perfectly pure and suitable for the preparation of dyes. Yield of phenobromide of 4-methyldihydrobenzohepta-1,5-thiazine 3 g (87%).

Found %: Br 24.05. $C_{16}H_{16}NSBr$. Calculated %: Br 23.93.

The phenoperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine, prepared in the usual manner from the phenobromide of 4-methyldihydrobenzohepta-1,5-thiazine and perchloric acid, was isolated in crystalline form. It has m.p. 163° and is identical with the phenoperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine that we previously prepared [1] from 4-methyl-5-phenyldihydrobenzohepta-1,5-thiazine and perchloric acid.

SUMMARY

1. A new method is proposed for preparation of quaternary salts of seven-membered heterocyclic compounds which consists in condensation of N-alkyl- and N-phenyl-o-aminophenylmercaptans with β-haloketones. It can be recommended as a preparative method for quaternary salts of the dihydrobenzohepta-1,5-thiazine series.

2. The new method was employed for the preparation of 4 new quaternary salts in the dihydrobenzohepta-1,5-thiazine series which had not previously been described in the literature.

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Kiev State University Received January 31, 1957

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*Original Russian pagination. See C. B. Translation.

REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

VII. REACTION OF DIAZO COMPOUNDS WITH UNSUBSTITUTED SULFAMIC ACID

D.Z. Zavel'skii and L.A. Lishnevskaia

It was previously [1] shown that unsubstituted sulfamic acid reacts only with active diazo compounds, i.e. those containing electron-accepting groups (NO_2, Cl, etc.). This does not lead, however, to the expected aryltriazene-N-sulfonic acids but to the amine or symmetrical diaryltriazene corresponding to the diazo compound. We explained this reaction by a scheme whereby unstable aryltriazene-N-sulfonic acids are first formed and slowly break down to give nitrogen, sulfur trioxide and amine; if the amine is sufficiently active in the diazoamino condensation, it is capable of forming a symmetrical diaryltriazene with the diazo compound present.

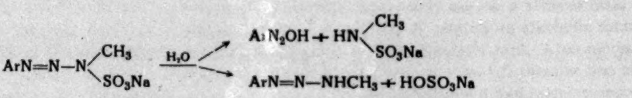
$$ArN_2OH + NH_2SO_3Na \rightarrow ArN{=}N{-}NHSO_3Na + H_2O \qquad (1)$$

$$ArN{=}N{-}NHSO_3Na \xrightarrow{H_2O} ArN{=}N{-}NH_2 + HOSO_3Na \qquad (2)$$

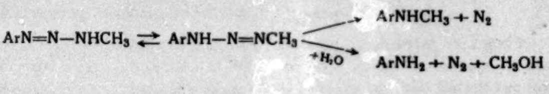
$$ArN{=}N{-}NH_2 \rightarrow ArNH_2 + N_2 \qquad (3)$$

$$ArNH_2 + ArN_2OH \rightarrow ArNH{-}N{=}NAr + H_2O \qquad (4)$$

The correctness of the above mechanism was confirmed by the fact that by reaction of diazo compounds with N-methylsulfamic acid we obtained [2] products of the diazoamino condensation—methylaryltriazene-N-sulfonates—which had adequate stability but were susceptible to breakdown in an acid medium in the following manner:

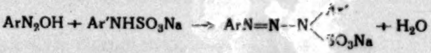


$$ArN{=}N{-}N\begin{matrix}CH_3\\SO_3Na\end{matrix} \xrightarrow{H_2O} \begin{cases} ArN_2OH + HN\begin{matrix}CH_3\\SO_3Na\end{matrix} \\ ArN{=}N{-}NHCH_3 + HOSO_3Na \end{cases} \qquad (5)$$

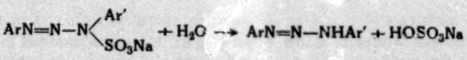


$$ArN{=}N{-}NHCH_3 \rightleftarrows ArNH{-}N{=}NCH_3 \begin{cases} \rightarrow ArNHCH_3 + N_2 \\ \xrightarrow{+H_2O} ArNH_2 + N_2 + CH_3OH \end{cases} \qquad (6)$$

Further confirmation of the proposed mechanism of reaction of diazo compounds with unsubstituted sulfamic acid was afforded by our study [3] of the reaction of formation and breakdown of labile diaryltriazene-N-sulfonates with formation of unsymmetrical diaryltriazenes.



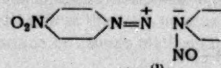
$$ArN_2OH + Ar'NHSO_3Na \rightarrow ArN{=}N{-}N\begin{matrix}Ar'\\SO_3Na\end{matrix} + H_2O \qquad (7)$$



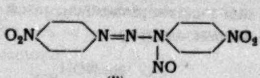
$$ArN{=}N{-}N\begin{matrix}Ar'\\SO_3Na\end{matrix} + H_2O \rightarrow ArN{=}N{-}NHAr' + HOSO_3Na \qquad (8)$$

Grimmel and Morgan [4] used sulfamic acid as the agent for removal of excess of nitrous acid during diazotization of amines [5] and also observed that it reacts with very negatively substituted diazo compounds in an acid medium with formation of nitrogen, sulfuric acid and starting arylamine. The authors considered three variants of an explanation of the mechanism of the reaction and reached the conclusion that the most probable mechanism is that advanced above (Equations 1 to 3).

Other conclusions may be reached on the basis of the work of I. V. Grachev and B. A. Porai-Koshits [6]. These authors found that in a neutral medium diazo compounds release nitrous acid with formation of diaryltriazenes. On the basis of this observation and of the results of potentiometric titration, the authors concluded that in a neutral medium diazo compounds exist as salts [diazonitrosaminates (I)] or covalent compounds [diaryl-N-nitrosotriazenes (II)].



(I)

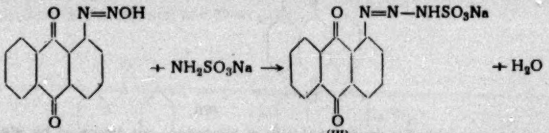


(II)

In the authors' opinion, these compounds are capable of splitting off the nitroso group just as easily as diaryltriazene-N-sulfonates split off the sulfo group. In the light of the ideas of I. V. Grachev and B. A. Porai-Koshits, it is logical to assume that sulfamic acid differs from its monosubstituted derivatives in not entering into the diazoamino condensation with diazo compounds according to reaction (1) and that it is only an acceptor of nitrous acid which splits off from compounds of the type of (I) and (II).

Wishing to obtain direct proof of the ability of unsubstituted sulfamic acid to undergo the diazoamino condensation and having obtained negative results with diazo compounds of the benzene series, we tried to bring it into reaction with 1-diazoanthraquinone. This attempt was prompted by the known fact that no diazo compound of the benzene series is capable of forming the corresponding stable triazenes with ammonia, hydroxylamine or hydrazine, whereas 1-diazoanthraquinone (as well as some derivatives) is capable of giving triazenes with these substances, as was shown by Wacker [7].

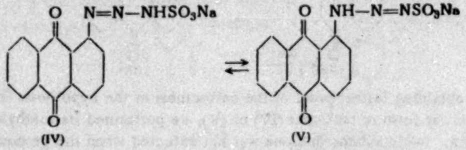
Experiment showed that at a pH of 6 to 8.5 it is possible to condense 1-diazoanthraquinone with sulfamic acid to give an 80–85% yield of 1-anthraquinonyltriazene-3-sulfonate (III).



(III)

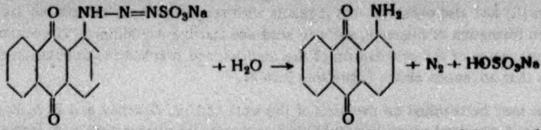
(9)

After recrystallization from water the product is free of sodium acetate, but is unstable in storage and when heated in the dry form or in aqueous solution. On decomposition it forms 1-aminoanthraquinone, bisulfate and nitrogen. The same products result immediately on addition of mineral acid to the cold aqueous solution of the triazene; the same process occurs, but slowly, when acetic acid is added. The decomposition of 1-anthraquinonyltriazene-N-sulfonate is readily accounted for by the hypothesis that the triazene with the structure (IV) (as indicated by the synthesis) undergoes tautomeric rearrangement to form (V) which irreversibly breaks down according to equation (11), so that equilibrium (10) is shifted to the right.



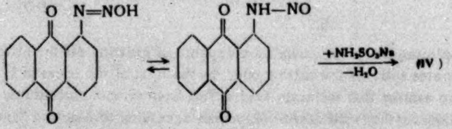
(IV) (V)

(10)

 (11)

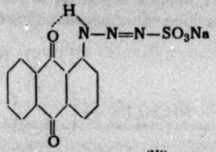
The experiment with 1-diazoanthraquinone has thus afforded direct proof that unsubstituted sulfamic acid is capable of reacting with diazo compounds in the capacity of an amino component and not in the capacity of an acceptor of nitrous acid.

The hypothesis that 1-diazoanthraquinone reacts with sulfamic acid in the form of a nitrosamine with formation directly of the tautomer (IV)

 (12)

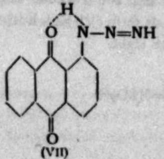
must be considered unproven since on prolonged stirring of specially synthesized ethylphenylnitrosaminate [8] and ethyl-(4-nitrophenyl)-nitrosaminate [9] in aqueous or aqueous alcoholic solution with sodium sulfamate we failed to observe any signs of the formation of a triazene.

It was found that 1-anthraquinonyltriazene-N-sulfonate is incapable of coupling with hydroxy- or aminoazo components in a medium of acetic acid or mineral acid in a similar manner to ordinary triazenes. On this basis we may suggest that the tautomer (IV), formed during synthesis, isomerizes to (V) in which the proximity of the anthraquinone carbonyl causes the compound to be stabilized in the form of (VI) with a hydrogen bond.

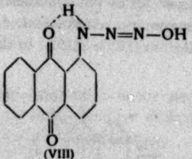


(VI)

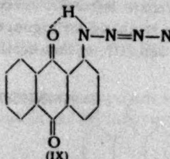
This hypothesis may account for the incapability of existence, not discussed by Wacker [7], of products of the diazoamino condensation of diazo compounds of the benzene series with ammonia, hydroxylamine and hydrazine, whereas the corresponding derivatives of α-diazoanthraquinone are quite stable. In this case also we can suggest that these anthraquinonyltriazenes are stabilized by the formation of a hydrogen bond between the labile hydrogen of the triazene group and the carbonyl oxygen.



(VII)

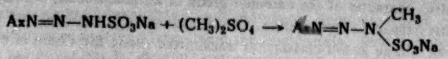


(VIII)

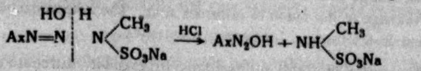


(IX)

With the objective of obtaining further proof of the correctness of the hypothesis that 1-anthraquinonyltriazene-N-sulfonate exists in the form of tautomer (IV) or (V), we performed its methylation with dimethyl sulfate in an alkaline medium. 1-Diazoanthraquinone was not detected when the product of methylation was acidified. The reaction accordingly did not proceed according to the scheme:

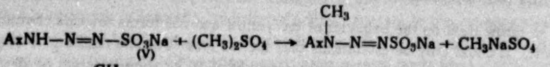


$$\mathrm{AxN{=}N{-}NHSO_3Na + (CH_3)_2SO_4 \longrightarrow AxN{=}N{-}N}\begin{smallmatrix}\mathrm{CH_3}\\ \mathrm{SO_3Na}\end{smallmatrix}$$

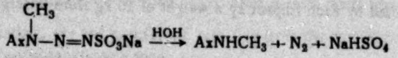


$$\mathrm{AxN{=}N}\overset{\mathrm{HO}\;\mathrm{H}}{\Big|}\mathrm{N}\begin{smallmatrix}\mathrm{CH_3}\\ \mathrm{SO_3Na}\end{smallmatrix} \xrightarrow{\mathrm{HCl}} \mathrm{AxN_2OH + NH}\begin{smallmatrix}\mathrm{CH_3}\\ \mathrm{SO_3Na}\end{smallmatrix}$$

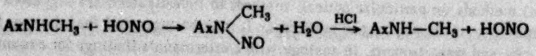
The red product coming down on acidification was a mixture of 1-methylaminoanthraquinone and 1-aminoanthraquinone. Treatment of the mixture with nitrite in concentrated hydrochloric acid gave 1-diazoanthraquinone, which went into solution, and a nitroso derivative of 1-methylaminoanthraquinone which remained undissolved. The nitroso product gave a positive reaction in the Liebermann test. Hydrolysis of the nitroso product with concentrated hydrochloric acid at the boil gave 1-methylaminoanthraquinone whose melting point was the same as that of a mixture (165–167°) with an authentic specimen of 1-methylaminoanthraquinone synthesized by Lauer's method [10]. The reactions



$$\underset{\mathrm{(V)}}{\mathrm{AxNH{-}N{=}N{-}SO_3Na}} + \mathrm{(CH_3)_2SO_4} \longrightarrow \mathrm{Ax}\overset{\mathrm{CH_3}}{\mathrm{N}}\mathrm{{-}N{=}NSO_3Na + CH_3NaSO_4} \qquad (13)$$



$$\mathrm{Ax}\overset{\mathrm{CH_3}}{\mathrm{N}}\mathrm{{-}N{=}NSO_3Na} \xrightarrow{\mathrm{HOH}} \mathrm{AxNHCH_3 + N_2 + NaHSO_4} \qquad (14)$$

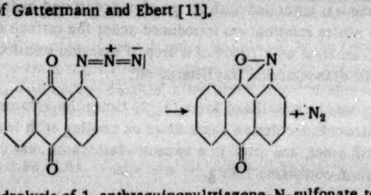


$$\mathrm{AxNHCH_3 + HONO \longrightarrow AxN}\begin{smallmatrix}\mathrm{CH_3}\\ \mathrm{NO}\end{smallmatrix} + \mathrm{H_2O} \xrightarrow{\mathrm{HCl}} \mathrm{AxNH{-}CH_3 + HONO} \qquad (15)$$

confirm that 1-anthraquinonyltriazene-N-sulfonate exists in the form of the tautomer (V) or (VI). During methylation of the triazene it was noted that it dissolves in dilute alkali with a dark-red color and after a short time it deposits a light-brown substance. It was established that even at room temperature alkali nearly quantitatively cleaves 1-anthraquinonyltriazene-N-sulfonate into anthraquinonyl azide and sulfurous acid:

$$\mathrm{AxNH{-}N{=}NSO_3Na \longrightarrow AxN_3 + HSO_3Na} \qquad (16)$$

1-Anthraquinonyl azide was identified by its appearance (stout, brownish-yellow needles), elementary analysis, and reactions, the most characteristic of which is the transformation into anthranyl by a slight modification of the procedure of Gattermann and Ebert [11].

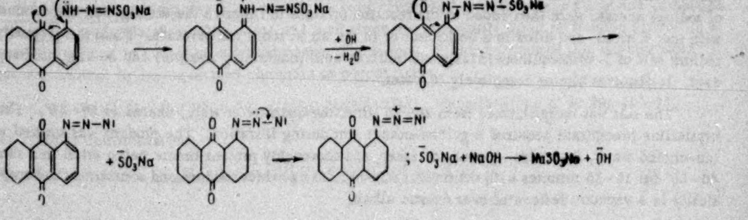


(17)

The smooth and facile hydrolysis of 1-anthraquinonyltriazene-N-sulfonate to 1-anthraquinonyl azide and sulfur dioxide is similar in character to the hydrolysis with alkali of the products of coupling of diazo compounds with aryl- or alkylsulfamides to form aryl azides and sulfinic acid. The latter reaction was studied by Dutt and co-workers [12].

$$\mathrm{ArN{=}N{-}NHSO_2R} \xrightarrow{\mathrm{NaOH}} \mathrm{ArN_3 + RSO_2H} \qquad (18)$$

It is an example of a nucleophilic substitution reaction. We put forward the following reaction mechanism:



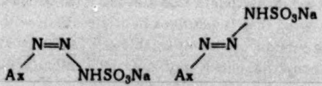
Due to the electrophilic character of the carbonyl group of anthraquinone, a positive charge is at first formed at the nitrogen. This causes the hydrogen at the nitrogen to be protonized and to react with hydroxyl to form water. The negative charge at the carbonyl is transmitted along the chain of conjugated bonds to the end nitrogen, resulting in cleavage of the anion of sulfurous acid. The anthraquinonyl residue with three conjugated nitrogens is stabilized in the form of 1-anthraquinonylazide.

Consequently, under the action of alkali anthraquinonyltriazene-N-sulfonate undergoes an intramolecular oxidation–reduction reaction, the sulfo group being reduced to sulfurous acid while the anthraquinonyltriazene residue is oxidized to anthraquinonyl azide.

The two forms of 1-anthraquinonyltriazene-N-sulfonate. It was recalled earlier that freshly recrystallized triazenesulfonate (yellow) fairly quickly turns red in storage. The red product is completely soluble in water, but both in the dry state and in solution it is very much less stable than the yellow form, and tends even without acidification to break down to 1-aminoanthraquinone, nitrogen and sulfur trioxide. The light-red form is more soluble than the yellow form in alcohol.

All attempts to throw light on the behavior of the yellow and red forms towards chemical reagents remained without result. It could only be established that the red form was less resistant to impact than the yellow; the former is decomposed by each impact by a weight of 10 kg from a height of 20 cm, while the second form is not.

Physicochemical methods, in particular optical methods of investigation are suggested for clarification of the difference in structures of the yellow and red forms. It may be suggested that the two forms of the triazenesulfonate are cis- and trans-isomers, in analogy with Gattermann's findings for azoanthraquinone [11].



EXPERIMENTAL

Diazotization of 1-aminoanthraquinone. Schaarschmidt's procedure [13] was used with slight modifications. 2.21 g of 1-aminoanthraquinone was triturated with 20 ml of concentrated hydrochloric acid. After 10-minutes' stirring, 2.2 ml of 5 N sodium nitrite solution was introduced under the surface of the liquid at room temperature. After red amine had ceased to separate on dilution of a drop of reaction solution with water, the reaction mass was cooled and the precipitated diazochloride was filtered off.

The diazochloride slurry was recrystallized from 15–20 times the volume of water at 60–70°. Large crystals of 1-anthraquinonyl diazonium chloride came down on cooling with ice. They were filtered, washed with cold alcohol and then with ether, and dried in a vacuum-desiccator over caustic alkali and paraffin wax. Yield of recrystallized diazonium compound 1.63 g.

Condensation of 1-diazoanthraquinone with sulfamic acid. 2.38 g of sodium sulfamate was dissolved in 10 ml of concentrated acetate buffer with a pH of 6; a solution of 2.7 g of 1-anthraquinonyl diazonium chloride saturated at room temperature was then added in one portion. The reaction mass gradually deposited a light-brown precipitate. The pH of the mixture was brought to 8.0–8.5 by addition of bicarbonate and subsequently kept at this level. The pH of the solution ceased to fall in 1–2 hours after the start of the experiment, and the compound ceased to give a reaction for an active diazo compound with H-acid, although the precipitate from the reaction mixture only ceased to give an active diazo reaction after stirring for 16–18 hours. A few grams of sodium acetate were then added to the reaction mixture to improve the salting-out; the product was cooled with ice, filtered, and dried in a desiccator or in the air at room temperature. Yield 3.5 g (purity 81.2%). The sodium salt of 1-anthraquinonyltriazene-3-sulfonic acid (containing acetate) can be kept unchanged for several days. It dissolves almost completely in water.

The salt was recrystallized from 20–25 times the quantity of water heated to 50–55°. The yellow, crystalline precipitate acquired a golden-orange tint during filtration. The product was washed with initially ice-cooled water, then with alcohol and ether, and thoroughly pressed before being dried in a thermostat at 40–50° for 10–15 minutes with continuous stirring. The product reddens and sometimes decomposes if dried slowly in a vacuum-desiccator over caustic alkali.

Properties of sodium 1-anthraquinonyltriazene-3-sulfonate. Lustrous, yellow or golden-orange crystals with the form of flat needles or elongated plates under the microscope. Readily soluble in water (the solution has a yellow color), less easily soluble in alcohol, and very sparingly soluble in ether.

In the pure form the sodium salt of the triazene-N-sulfonic acid is remarkably unstable. Preparations can with luck be kept in vacuo at room temperature for some hours without change. They often decompose, however, even during drying or a few minutes after drying. A sign of the start of breakdown is reddening, while the completion of decomposition is marked by conversion into a water-insoluble product. At the same time the compound gives off nitrogen, and the substance develops an acid reaction to Congo. An aqueous extract of the decomposed product gives an abundant precipitate of barium sulfate with barium chloride.

Heating of the dry preparation to 50–60° in an open test tube leads to instantaneous decomposition, and drops of water are deposited on the walls.

Heating of an aqueous solution of the triazene sulfonate to above 50° causes it to gradually turn bright-red, and a gel of fine precipitate is formed. Addition of sodium acetate to the aqueous solution raises the temperature of decomposition. A red precipitate comes down quickly when mineral acid is added to a cold solution of the triazene. The same decomposition occurs after several hours when acetic acid is added.

After one recrystallization, the red precipitate resulting from decomposition of the triazene sulfonate has m.p. 246°. It is very pure 1-aminoanthraquinone.

The triazene-N-sulfonate does not couple with azo components either in neutral, acetic acid or mineral acid media.

Analysis of sodium anthraquinonyltriazene-N-sulfonate. Water of crystallization. A weighed sample was put into a crucible with a lid and left to break down spontaneously. The crucible was then placed in a thermostat at 110° until the weight was constant.

The calculation was based on the equation of decomposition:

$$C_6H_4(CO)_2C_6H_3N_2-NHSO_3Na \cdot nH_2O = C_6H_4(CO)_2C_6H_3NH_2 + NaHSO_4 + N_2 + (n-1)H_2O.$$

Found %: loss of weight 15.06, 15.36. With n = 3, calculated %: loss of weight 15.72.

The compound therefore contains 3 molecules of water of crystallization.

Diazo nitrogen. A weighed sample of the substance was placed in the flask of an apparatus for determination of diazo nitrogen and several milliliters of concentrated sodium acetate solution were added. Air was flushed out of the apparatus with carbon dioxide, after which 50 ml of 50% sulfuric acid was poured into the flask. The solution quickly turned red and an upper layer of 1-aminoanthraquinone was formed. Nitrogen was driven off by boiling.

Found %: diazo nitrogen 6.88, 6.81. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: diazo nitrogen 6.88.

Sodium. The residue in the flask after determination of crystal water was moistened with sulfuric acid and ashed.

Found %: Na 5.62, 5.57. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: Na 5.65.

Sulfur (by Carius and Messinger methods).

Found %: S 8.05, 7.92. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: S 7.87.

Carbon and hydrogen. A tube was filled with fused lead chromate. A weighed sample of the compound was mixed with pulverized potassium dichromate and lead chromate (previously dried by heating to 700° in a nitrogen stream) and placed in a boat of oxidized copper 20 cm long. Small portions of this mixture were separated from one another by layers of lead chromate or copper oxide.

Found %: C 41.48, 41.43; H 3.27, 3.32. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: C 41.28; H 3.47.

Nitrogen (Dumas determination).

Found %: N 10.37, 10.21. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: N 10.32.

Methylation of sodium 1-anthraquinonyltriazene sulfonate. 4.07 g of the compound was suspended in 20 ml of water, and 6.3 g of dimethyl sulfate, previously treated with sodium carbonate until the acid reaction had disappeared, was run in. During the methylation an alkaline reaction was maintained by gradual addition of sodium hydroxide. After it had been stirred for 8 hours, the alkaline solution was left overnight. The resulting light-brown, viscous mass was acidified with hydrochloric acid while heating. The red precipitate was filtered off. The filtrate did not couple with azo components and did not take up nitrite; therefore it did not contain diazoanthraquinone and sulfamic (or methylsulfamic) acid. The red precipitate was washed, pressed, mixed with concentrated hydrochloric acid and treated with excess of 5 N nitrite. Part of the solid went into solution and part acquired a sandy color. The reaction mixture was filtered. 1-Diazoanthraquinone was detected in the filtrate (coupling with R-salt). The precipitate was washed with hydrochloric acid, then with water (until the reaction for nitric acid was absent) and dried. It then weighed 0.7 g. On fusion of a sample with phenol and sulfuric acid, the melt became intensely green; when the melt was poured into water the mixture turned red, while addition of alkali changed the color to blue. With diphenylamine in sulfuric acid a sample of the precipitate gave a deep-blue coloration. Both of the reactions identify the substance as a nitrosamine.

0.5 g of the nitrosamine was hydrolyzed by boiling with 5 ml of concentrated hydrochloric acid. The light-brown suspension darkened and went into solution with a brownish-red color. The small quantity of dark precipitate was filtered and 50 ml of water was added to the filtrate. A dark-red flocculent precipitate came down and the liquid became nearly colorless. The precipitate was filtered, washed with water and dried. After recrystallization from alcohol and then from benzine it had m.p. 165–167°. A mixture with authentic 1-methylaminoanthraquinone (m.p. 166°) melted at 165–167°. Consequently hydrolysis of the nitroso product had led to formation of methylaminoanthraquinone.

Reaction of sodium 1-anthraquinonyltriazene sulfonate with alkali. a) Preparation of 1-anthraquinonyl azide. To 4.07 g of the triazene sulfonate, mixed with 120 ml of water, was added 3-4 ml of 40% sodium hydroxide. The reaction mixture turned dark-red, and the solid went into solution after a few minutes. A dark substance started to come down quickly. In an hour after addition of the alkali, the solid was filtered off, washed with water and dried in the air. The light-brown product weighed 3.36 g. Careful recrystallization from hot methanol in presence of active carbon gave brownish-yellow needles (under the microscope the crystals had the form of stout needles and elongated prisms). For analytical purposes it was recrystallized again from methanol and dried in a vacuum-desiccator over potassium hydroxide.

Found %: N 16.62, 16.47. $C_{14}H_7O_2N_3$. Calculated %: N 16.86.

After a few days in the air or a desiccator, the lustrous crystals became dull and crumbly. Examination under the microscope revealed, apart from yellow needles and prisms of azide, fine crystals of indeterminate form and with a deeper reddish tone.

b) Determination of sulfur dioxide. A weighed sample of the triazene was stirred with 8 ml of water and 0.8 ml of 40% sodium hydroxide solution at 50–60° for 20 minutes. A precipitate came down on cooling and was filtered. The filtrate was acidified with sulfuric acid and the sulfur dioxide was driven off into alkali solution. The SO_2 content of the distillate was determined by iodometry.

Found %: SO_2 15.9. $C_{14}H_8O_5N_3SNa \cdot 3H_2O$. Calculated %: SO_2 15.7.

c) Conversion of 1-anthraquinonyl azide into anthranil (benzopseudoxazole). A weighed sample of anthraquinonyl azide was placed in a small flask connected to a nitrometer filled with potassium hydroxide solution. 50 ml of xylene was added, air was purged out of the system by a stream of CO_2, and the mixture was heated to the boil. Evolution of gas was complete after boiling for 5 minutes.

Found %: diazo nitrogen 10.5. $C_{14}H_7O_2N_3$. Calculated %: diazo nitrogen 11.24.

Crystals were deposited from the xylene solution remaining in the flask. They were filtered, washed and dried. Under the microscope they appeared as stout, orange prisms. They did not have a sharp melting point.

Found %: N 6.44. $C_{14}H_7O_2N$. Calculated %: N 6.33.

A specimen of the anthranil was heated with concentrated sulfuric acid and the solution was poured on to ice. The resulting dark-red precipitate was identified as 1-amino-4-hydroxyanthraquinone. This reaction is characteristic of anthranil [7, 11].

The two forms of sodium anthraquinonyltriazene-N-sulfonate. On recrystallization of the triazene from water at 55°, a yellow suspension was obtained which consists of yellow, elongated plates. During filtration the substance turned pink with a tinge of gold. The substance became a deeper red after pressing between sheets of filter paper and drying in a vacuum-desiccator over solid alkali. However, the form of the crystals and their ability to dissolve completely in water remained unchanged. If the light-red product was treated with alcohol before drying, the alcohol acquired an orange color and the solid again turned yellow. After filtration, washing with ether, and drying for 1.5 hours in a vacuum-desiccator, the egg-yellow product again turned red and approached the color of the basic product prior to treatment with alcohol. This reddened product was likewise completely soluble in water, but its aqueous solution was very unstable. After only a few minutes it started to give off nitrogen and deposited red 1-aminoanthraquinone. After the reddened product had been in a desiccator for several hours, and had then been treated with alcohol, intensive evolution of nitrogen commenced and aminoanthraquinone came down.

The light-red product was kept for 2.5 hours in the desiccator and then treated with alcohol. The resulting yellow product was filtered and recrystallized from water. During filtration, pressing and drying, the crystals again acquired a light-red color with a golden tinge. The operations of treatment with alcohol and recrystallization could be repeated many times to give, from the same substance, sometimes the egg-yellow and sometimes the light-red form of the triazene-N-sulfonate.

It was established that the yellow form is appreciably more stable in store than the red form. In some experiments the yellow form that had been kept in a vacuum-desiccator remained completely soluble in water for 24 hours although it turned slightly red. The red form of the triazene prepared from the identical starting substance decomposed under these conditions in the course of 2–3 hours.

It was observed that 1-anthraquinonyltriazene-N-sulfonate decomposes instantaneously under impact with formation of 1-anthraquinone which becomes enveloped in a red cloud due to the vigorous release of nitrogen. The yellow and red forms of the substance were tested for sensitivity to shock with the help of a drop hammer usually employed for testing of explosives. It was found that with a load of 10 kg and a height of fall of 20 cm the red substance is decomposed with formation of 1-aminoanthraquinone 25 times out of 25 tests. Under these conditions the yellow form began to decompose only after turning red in storage. Consequently the yellow form is more resistant than the red form to shock and to spontaneous decomposition.

SUMMARY

1. A mechanism of the reaction between diazo compounds and unsubstituted sulfamic acid is put forward and discussed. It postulates the initial formation of an aryltriazene-N-sulfonic acid which tautomerizes to a labile form which breaks down to arylamine, nitrogen and sulfuric acid.

2. The proposed mechanism was confirmed by the synthesis of 1-anthraquinonyltriazene-3-sulfonate by condensation of 1-diazoanthraquinone with sulfamic acid and by the susceptibility of this triazene to facile breakdown to 1-aminoanthraquinone, nitrogen and sulfuric acid.

3. It is suggested that the greater stability of 1-anthraquinonyltriazene-N-sulfonate in relation to its benzenoid analogs is due to the circumstance that the labile hydrogen of the triazene group is located at the nitrogen adjacent to the anthraquinonyl residue and forms a hydrogen bond with the carbonyl group of anthraquinone.

4. The location of the labile hydrogen at the nitrogen adjacent to the anthraquinonyl residue is proven by the breakdown of 1-anthraquinonyltriazene-3-sulfonate to aminoanthraquinone, nitrogen and sulfur trioxide, as well as by the formation of 1-methylaminoanthraquinone on breakdown of the product of methylation of this triazene.

5. It was found that 1-anthraquinonyl-3-sulfonate readily splits into 1-anthraquinonyl azide and sulfur trioxide under the action of alkali. This reaction is regarded as a nucleophilic substitution under the action of the hydroxyl ion.

6. It was established that sodium 1-anthraquinonyltriazene-3-sulfonate exists in a yellow and a red form, the first of which is the more stable.

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Received March 30, 1957

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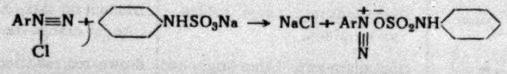
* Original Russian pagination. See C. B. Translation.

REACTIONS OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

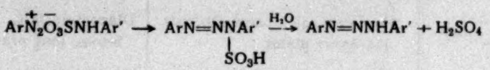
VIII. DIAZONIUM SALTS OF ARYLSULFAMIC ACIDS

D. Z. Zavel'skii and L. A. Lishnevskaia

In the preceding communication [1] we pointed out that salts of diazo compounds in aqueous solutions with a pH of 2 to 5 enter into exchange reaction with sodium benzenelsulfamate with formation of aryldiazonium benzenesulfamates.



These salts later rearrange gradually, especially when the pH of the reaction medium is increased, to the unstable diaryltriazene-N-sulfonic acids which cannot be isolated due to their tendency to split off the labile sulfo group attached to the nitrogen with formation of diaryltriazenes.

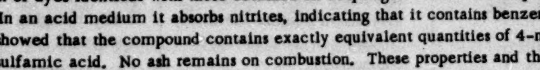


$$\mathrm{Ar\overset{+}{N}_2\overset{-}{O}_3SNHAr'} \longrightarrow \mathrm{ArN{=}N\underset{SO_3H}{\underset{|}{}}Ar'} \xrightarrow{H_2O} \mathrm{ArN{=}NHAr'} + \mathrm{H_2SO_4}$$

It was found that benzenediazonium sulfamates differ from the majority of known diazonium salts in being deeply colored. For example the mixing of colorless solutions of 4-nitrobenzenediazonium chloride and sodium benzenesulfamate at a pH of 2 to 5 results in the reaction mass becoming deep brownish-red and in rapid deposition of deep reddish-brown, lustrous crystals. The latter were moderately soluble in water with a neutral reaction and could be recrystallized from 10% acetic acid. They are poorly soluble (with decomposition) in organic media; in the dry state they deflagrate on heating; they are stable when kept for 3–5 days, after which they darken, split off sulfuric acid and develop an odor of phenol.

An aqueous solution of the brownish crystals couples in a neutral medium with azo components (H-acid, P-salt) with formation of dyes identical with those obtained on coupling of these azo components with 4-nitrobenzenediazonium. In an acid medium it absorbs nitrites, indicating that it contains benzenesulfamic acid. Qualitative analysis showed that the compound contains exactly equivalent quantities of 4-nitrobenzenediazonium and benzenesulfamic acid. No ash remains on combustion. These properties and the elemental composition confirmed that the investigated product was the 4-nitrobenzenediazonium salt of benzenesulfamic acid.

Well-formed and deeply colored crystals of diazonium salts of benzenesulfamic acid are also formed by many other diazo compounds on reaction with benzenesulfamic acid, the products easily coming down from water. In properties they closely resemble the above-described 4-nitrobenzenediazonium salt. It is interesting that saturated solutions of all of these colored salts, which are also fairly deeply colored, become weak-yellow when diluted. We can therefore infer that the colored benzenediazonium sulfamates again form colorless ions on dissociation in water.

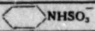
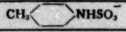
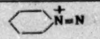
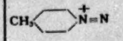
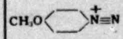
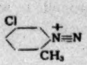
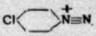
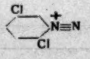
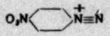
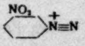
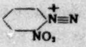
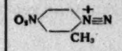
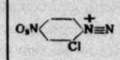
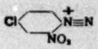
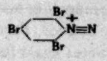


It is well-known that in the solid form the sulfates and arylsulfonates of the same diazo compounds are colorless or faint-yellow. The unusual properties of the benzenesulfamates therefore prompted us to synthesize a series of salts from diazo compounds of the benzene series and two arylsulfamic acids in order to establish how their color and some other properties change in dependence on the character and number of substituents in both of the benzene rings.

Diazochlorides were synthesized from 12 amines: aniline, 4-toluidine, 4-anisidine, 2-methyl-5-chloroaniline, 4-chloroaniline, 2,5-dichloroaniline, 4-nitroaniline, 3-nitroaniline, 2-nitroaniline, 2-methyl-4-nitro-

TABLE 1

Characteristics of Products of Reaction of Diazonium Chlorides with Sodium Salts of Arylsulfamic Acids

Preparation No.	Structure of diazonium	Structure of arylsulfamate anion	
			
1		Yellow solution. No precipitate.	Yellow solution. No precipitate.
2		Yellow-orange solution. No precipitate formed.	Yellow-orange solution. No precipitate formed.
3		Brown-orange solution. No precipitate.	–
4		Orange solution. No precipitate.	–
5		Diazonium salt. Large, golden, scaley plates.	Diazonium salt. Large, lustrous, bright orange-red plates.
6		Diazonium salt. Large bright-red needles.	Brown-red reaction mixture deposits the diazoamino compound slightly contaminated with diazonium salt which could not be isolated pure.
7		Diazonium salt. Large, lustrous, red-brown plates.	Diazonium salt. Very dark violet-brown, long plates.
8		Diazonium salt. Bright-orange plates with tapered corners.	Diazonium salt. Large, lustrous, red plates.
9		Diazonium salt hardly comes down from dark red-brown reaction mass.	Diazonium salt. Large, elongated, very dark-claret plates.
10		Diazonium salt. Large, brown prisms with pointed ends.	Diazonium salt. Lustrous, dark-brown (violet tinge), stout prisms.
11		Chocolate-colored diazonium salt comes down from the dark-brown solution and slowly changes into the diazoamino compound.	Diazonium salt. Black, elongated plates with a violet tinge. Unstable, easily changing into the diazoamino compound.
12		Diazonium salt. Claret-brown plates. Unstable. Easily change to the diazoamino compound.	Diazonium salt. Chocolate-brown elongated plates. The salt is unstable but slightly more stable than the benzenesulfamate.
13		Diazoamino compound containing only traces of diazonium salt comes down from the red-brown reaction mixture.	A mixture of diazonium salt and diazoamino compound comes down from the brown reaction mixture. The pure diazonium salt cannot be isolated.

aniline, 4-chloro-2-nitroaniline and 2,4,6-tribromoaniline. Their solutions in aqueous mineral acids were brought into reaction in the cold (after being freed from excess of nitrous acid) with sodium benzenesulfamate and sodium 4-toluenesulfamate. Results are summarized in Table 1.

The following conclusions can be drawn from the data of Table 1.

The color, solubility and stability of aryldiazonium sulfamates depend on the character of the substituents in the benzene rings of both the diazonium compounds and the arylsulfamic acids in the following manner: when the benzenediazonium ring does not contain a substituent or contains electron-donating substituents (H, 4-CH$_3$, 4-OCH$_3$) or one electron-donating and a second, relatively weakly electron-accepting, substituent (2-CH$_3$, 5-Cl), the resulting arylsulfamates are weakly colored, very easily soluble in water and free from a susceptibility to rearrange into triazenes.

If the substituents possess electron-accepting properties (4-Cl, 4-NO$_2$, 3-NO$_2$, 2-NO$_2$, 4,2-NO$_2$, CH$_3$), then the arylsulfamates are the more deeply colored the more electrophilic is the substituent in character or by virtue of its position; their solubility decreases to such an extent that they readily crystallize from solution (an exception is the deeply colored but highly soluble 2-nitrobenzenediazonium benzenesulfamate), while the tendency to rearrange into diazoamino compounds already becomes perceptible [1]. Finally, if the benzenediazonium ring contains two or three electron-accepting substituents (2,4-Cl, NO$_2$; 2,4-NO$_2$, Cl; 2,4,6-tribromo), then the arylsulfamates are even more deeply colored and so unstable that even in a mineral acid medium they rapidly rearrange to triazenes. The connecting link between the two latter groups of diazonium compounds is 2,5-dichlorobenzenediazonium, which with benzenesulfamic acid still forms quite a stable salt, whereas with toluenesulfamic acid it already mainly forms a diazoamino compound.

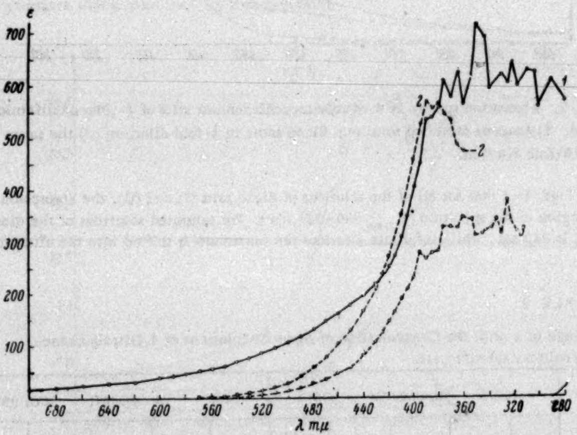


Fig. 1. Absorption spectra of 4-nitrobenzenediazonium salts of benzenesulfamic acid. 1) Aqueous saturated solution; 2) the same in 4-fold dilution; 3) the same in 10-fold dilution.

Whereas the presence of electron-donating groups in the benzenediazonium ring heightens the color of their arylsulfamates, the introduction of a methyl group into the 4-position of benzenesulfamic acid leads to deepening of color. Consequently, the lower the basicity of the diazonium cation and the acidity of the arylsulfamate anion, the more deeply colored are the salts formed by them.

It has already been remarked that although arylsulfamates of negatively substituted aryldiazoniums have very deep colors, their aqueous solutions (even when saturated) are more weakly colored. For example, solid 4-nitrobenzenediazonium benzenesulfamate forms deeply colored, red-brown crystals; its saturated solution (0.0775 M) has the color of tea, and more dilute solutions are light-yellow.

In order to obtain a closer insight into the properties of diazo compounds of arylsulfamates as colored substances, absorption spectra of aqueous solutions of four diazo salts of this series were obtained: 4-nitrobenzenediazonium benzenesulfamate and 4-toluenesulfamate, and 4-chlorobenzenediazonium benzenesulfamate and 4-toluenesulfamate (Figs. 1–4). Tables 2 and 3 contain the main numerical data characterizing the change of the molecular absorption coefficient ϵ with the concentration of aqueous solutions of the aryldiazonium sulfamates in the visible region of the spectrum.

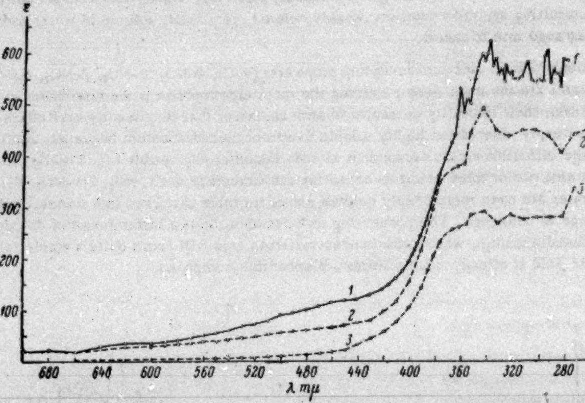
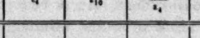
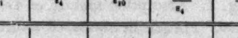


Fig. 2. Absorption spectra of 4-nitrobenzenediazonium salts of 4-toluenesulfamic acid. 1) Aqueous saturated solution; 2) the same in 4-fold dilution; 3) the same in 10-fold dilution.

We see from Figs. 1–4 that for all of the solutions of diazo salts (I) and (II), the absorption maximum is in the ultraviolet region of the spectrum (λ_{max} 340–360 mμ). For saturated solutions of the diazo compounds (III) and (IV) λ_{max} is 440 mμ, while for dilute solutions the maximum is shifted into the ultraviolet region of the spectrum.

TABLE 2

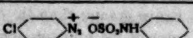
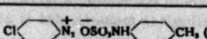
Change of ϵ with the Concentration of Aqueous Solutions of 4-Nitrobenzenediazonium Arylsulfamates

λ mμ	 (I)					 (II)				
	ϵ_1	ϵ_4	ϵ_{10}	$\frac{\epsilon_1}{\epsilon_4}$	$\frac{\epsilon_1}{\epsilon_{10}}$	ϵ_1	ϵ_4	ϵ_{10}	$\frac{\epsilon_1}{\epsilon_4}$	$\frac{\epsilon_1}{\epsilon_{10}}$
680	22	—	—	—	—	21	20	—	1.0	—
620	34	—	—	—	—	33	26	2.2	1.27	15.0
560	57	2.1	2.0	27.00	28.5	49	37	2.7	1.33	18.2
500	108	31	15	3.50	7.2	87	55	8.6	1.58	10.1
450	179	132	62	1.36	2.9	116	68	19.3	1.70	6.0
400	409	460	233	0.89	1.8	190	149	100	1.28	1.9

Notes. ϵ_1 is here and later the molar coefficient of absorption for the saturated solution; ϵ_4 is the coefficient in 4-fold dilution, and ϵ_{10} is the coefficient in 10-fold dilution. The molar concentration of the saturated solution (I) is 0.07757 M; the molar concentration of saturated solution (II) is 0.0893 M.

TABLE 3

Change of ε with the Concentration of Aqueous Solutions of 4-Chlorobenzenediazonium Arylsulfamates

λ mμ	 (III)			 (IV)				
	ε_1	ε_4	$\frac{\varepsilon_1}{\varepsilon_4}$	ε_1	ε_4	ε_{10}	$\frac{\varepsilon_1}{\varepsilon_4}$	$\frac{\varepsilon_1}{\varepsilon_{10}}$
680	2.8	1.6	1.75	1.3	–	—	—	—
620	3.3	1.7	1.94	1.5	0.4	—	3.75	—
560	4.6	1.7	2.7	2.9	0.8	—	3.6	—
500	10.1	2.4	4.2	13.9	4.3	1.5	3.23	9.3
450	24.4	6.4	3.8	40.8	13.7	6.6	3.0	6.2
400	21.8	16.4	1.33	40.5	34.2	21.4	1.18	1.9

Note. The molar concentration of the saturated solution (III) is 0.2406 M; that of saturated solution (V) is 0.1279 M.

Since the solid diazo salts (I) and (II) have a very dark color, the absence of λ_{max} from the visible spectrum is evidently due to dissociation of these salts into colorless ions at a relatively low molar concentration of their saturated solutions which were used for measurements.

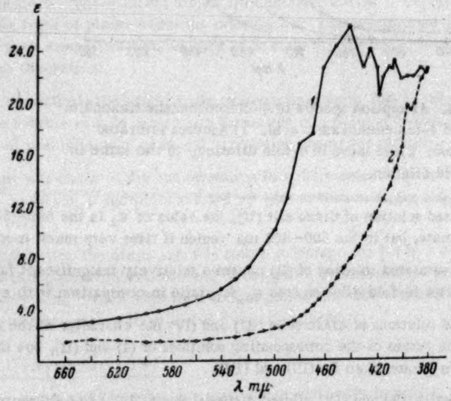


Fig. 3. Absorption spectra of 4-chlorobenzenediazonium salts of benzenesulfamic acid. 1) Aqueous saturated solution; 2) in 4-fold dilution.

Concerning diazo salts (III) and (IV), which are more highly colored in the solid form than (I) and (II), the λ_{max} of the saturated solutions is in the visible region of the spectrum, probably because their molar concentration is considerably greater than in the case of diazo salts (I) and (II).

Aqueous solutions of aryldiazonium sulfamates do not obey the Lambert-Beer law since their absorption coefficient is not proportional to the concentration.

The following conclusions can be drawn from the data of Tables 2 and 3.

1. For a saturated solution of diazo salt (I), ϵ_1 increases in the visible region from 22 at 680 mμ to 409 at 400 mμ. Such a course of the curve is characteristic of brown dyes.

2. A four-fold dilution of the saturated solution of (I) sharply reduces the molar coefficient of absorption: at 680 and 620 mμ it is difficult to measure, and at 560 mμ, ϵ_1 is 27 times greater than it. The lower the wavelength of the light the smaller the ratio of ϵ_1 to ϵ_2, so that the color of the solution approximates to yellow on dilution.

3. A 10-fold dilution of the saturated solution of (I) causes ϵ to fall even more sharply, but the ϵ_4/ϵ_{10} ratio is much smaller than ϵ_1/ϵ_4. Consequently, dissociation is already very considerable at 4-fold dilution.

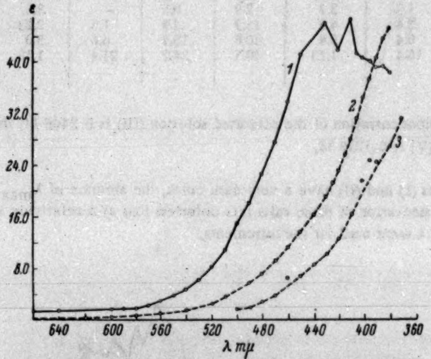


Fig. 4. Absorption spectra of 4-chlorobenzenediazonium salt of 4-toluenesulfamic acid. 1) Aqueous saturated solution; 2) the same in 4-fold dilution; 3) the same in 10-fold dilution.

4. In the case of a saturated solution of diazo salt (II), the value of ϵ_1 in the 680–500 mμ region is close to ϵ_1 of the benzenesulfamate, but in the 500–400 mμ region it rises very much more slowly.

5. A 4-fold dilution of a saturated solution of (II) causes a relatively insignificant fall in ϵ. Very much stronger dissociation is observed on 10-fold dilution (see ϵ_1/ϵ_{10} ratio in comparison with ϵ_1/ϵ_4 ratio).

6. In the case of saturated solutions of diazo salts (III) and (IV) the character of the absorption curves is little different from that of the curves of the corresponding solutions of (I) and (II), but the absolute value of ϵ for (I) and (II) is 5-20 times greater than for (III) and (IV).

7. For solutions of diazo salts (III) and (IV) diluted 4 times, the ϵ_1/ϵ_4 ratio characterizing the degree of dissociation of the diazo salts is slightly higher than for the corresponding solutions of the diazo salt (II) but considerably smaller than for diazo salt (I).

Consequently, the study of the absorption spectra of aryldiazonium sulfamates confirms the statement that the color characteristics of the latter are due to formation of undissociated salts. Dissolution of these salts and dilution of their solutions leads to dissociation of the colored salts into colorless cations and anions. The degree of dissociation evidently depends on the nature of the cation and anion of the salt.

EXPERIMENTAL

Synthesis of starting preparations. Sodium benzenesulfamate and sodium toluenesulfamate were prepared by the method described in [2] for benzenedisulfamic acid. 150 g of chlorosulfonic acid was gradually charged into 600 g of pyridine at -5 to 0°; this was followed, at a temperature not higher than 20°, by 93 g of aniline or 107 g of 4-toluidine. The mixture was heated to 60–70°, stirred for 2 hours, and (after cooling) neutralized with sodium carbonate solution. The pyridine was distilled off with steam and the solution was evaporated on a water bath and dried in a thermostat. The resulting powder was extracted with alcohol to eliminate inorganic salts. When the alcoholic solution was cooled it deposited sodium arylsulfamate in 88–96% purity, which was raised to 99.5–99.8% by two recrystallizations from alcohol. * The yield of arylsulfamates before recrystallization was about 80% of the theoretical on the basis of the original arylamine.

A solution of diazo compound was prepared by stirring of 0.01 mole of amine with 6 ml of 5 N hydrochloric acid at room temperature for half an hour, followed by addition of 7 g of crushed ice and (in one portion) 2.1 ml of 5 N sodium nitrite solution. The resulting diazo solution was filtered and the excess of nitrous acid was removed with a few drops of sulfamic acid solution, using as an indicator paper impregnated with methyl yellow solution. In the case of weakly basic amines (4-nitro-2-chloroaniline, 2,5-dichloroaniline, etc.) the hydrochloric acid proportion was 0.05 mole per 0.01 mole of amine, and the amount of nitrite was in 10% excess over the theoretical.

When it was necessary to obtain more concentrated diazo solutions, ice was not added to the mixture of amine and hydrochloric acid, its place being taken by external cooling with ice and salt.

Synthesis of diazonium salts of arylsulfamic acids. The sodium salt of the arylsulfamic acid was dissolved at 40–50° in 4 to 5 times as much water and then cooled externally with ice. The greater part of the salt came down. A little acetic acid was added to the suspension of arylsulfamate before the diazo solution was run in in order to bring the pH to 3.5–4.0.

4-Nitrobenzenediazonium benzenesulfamate. Addition of the diazo solution to the suspension of sodium benzenesulfamate resulted in the reaction mixture acquiring a brownish-red color, and in the disappearance of the white benzenesulfamate. The solution almost immediately started to deposit lustrous, large, brownish-red crystals which have the form of plates under the microscope. The precipitated 4-nitrobenzenediazonium arylsulfamate was nearly pure after filtration, washing with ether and drying in vacuo over potassium hydroxide. Yield about 87% of the theoretical.

For the purpose of analysis the product was recrystallized from 10% acetic acid heated to 50–55°. The red-brown crystals are soluble in cold water with formation of a pale-yellowish solution. The diazo salt easily dissolves in alcohol and glacial acetic acid and in so doing undergoes extensive decomposition.

When an attempt was made to dry the substance in a thermostat or by holding a sample on the tip of a spatula on an electric hotplate, it suddenly swelled up with evolution of gas and formation of a dark-grey, porous, carbonaceous mass.

Prior to recrystallization the diazo salt was stable in storage for 1.5 to 2 days, and after recrystallization for 4 to 6 days. After this period it darkened and developed a phenolic odor, while its aqueous solution was found to contain sulfuric acid. When kept for a longer period, the diazo salt changes into a dark amorphous mass no longer giving the reactions for an active diazo compound.

Analysis of the Diazonium Salt

Ash. A weighed sample of the substance was wetted with sulfuric acid in a crucible, carefully evaporated and ignited. No ash was detected.

Nitrogen (Dumas). Diazo salts are explosive. Combustion was therefore effected in a small boat of sheet copper 20 cm long and oxidized in the flame of a gas burner. The weighed sample of diazo salt was spread out in the boat in small portions which were separated by layers of fine copper oxide.

Found %: N 17.21, 17.35. $C_{12}H_{10}O_5N_4S$. Calculated %: N 17.39.

Diazo nitrogen. The sample of diazo salt was heated in 50% sulfuric acid. The liberated nitrogen was collected over potassium hydroxide solution.

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* The arylsulfamic acids could be analyzed by titration with nitrite in hydrochloric acid solution in presence of potassium bromide.

Found %: diazo nitrogen 8.61. $C_{12}H_{10}O_5N_4S$. Calculated %: diazo nitrogen 8.69.

Diazo cation. A weighed sample of diazo salt was dissolved in 150–200 ml of water and an excess of neutral standard solution of β-naphthol was added. The pH was brought to 7 by addition of bicarbonate, and after 30 minutes the excess of β-naphthol was determined by titration with a p-nitrobenzenediazonium solution.

0.5228 g of substance. Found: consumption of 0.1 N β-naphthol 15.95 ml. $C_{12}H_{10}O_5N_4S$. Calculated: consumption of β-naphthol 16.20 ml.

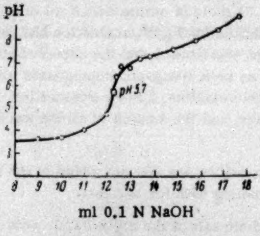

Fig. 5. Potentiometric titration curve of the 4-nitrobenzenediazonium salt of benzenesulfamic acid.

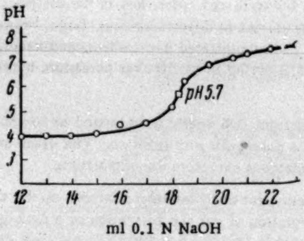

Fig. 6. Potentiometric titration curve of the 4-nitrobenzenediazonium salt of 4-toluenesulfamic acid.

Benzenesulfamate anion. The reaction mixture obtained after determination of the diazo cation was filtered from the β-naphthol azo dye. The filtrate and wash liquors were acidified with 25 ml of concentrated hydrochloric acid, 0.5 g of potassium bromide was added, and the benzenesulfamic acid was back-titrated with nitrite.

0.5228 g of substance: consumption of 0.1 N $NaNO_2$ 15.9 ml. $C_{12}H_{10}O_5N_4S$. Calculated: consumption of 0.1 N $NaNO_2$ 16.2 ml.

Potentiometric titration of the diazo salt. A weighed sample of the substance was dissolved in water, a small quantity of 0.1 N HCl was added, and the solution was titrated with 0.1 N NaOH, using a glass electrode (in the State Institute of Applied Chemistry type of pH-meter). The isoelectric point was found to lie at pH 5.7.

4-Nitrobenzenediazonium salt of 4-toluenesulfamic acid. After the diazo solution had been run into a suspension of sodium toluenesulfamate in water, the reaction mixture at once acquired a dark-brown color. A dark precipitate came down after a few minutes. It was filtered and recrystallized from water heated to 50–55°. Deeply colored violet-brown crystals were obtained with the appearance of elongated plates under the microscope. The color of the mother liquor was pale-yellow; after standing for 40 minutes it deposited a yellowish substance insoluble in water and not coupling with azo components in a neutral medium. This precipitate gave an intense coloration when heated in glacial acetic acid in presence of α-naphthylamine; it is therefore a diazoamino compound.

Found %: diazo nitrogen 8.10. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

Potentiometric titration of the diazo salt revealed an isoelectric point at pH 5.7.

3-Nitrobenzenediazonium salt of benzenesulfamic acid. An orange solid forming lustrous, bright-orange crystals after recrystallization from water heated to 50°. Plates with tapered corners under the microscope. The salt is soluble in cold water to give a yellowish-orange solution.

Found %: diazo nitrogen 8.40. $C_{12}H_{10}O_5N_4S$. Calculated %: diazo nitrogen 8.69.

3-Nitrobenzenediazonium salt of 4-toluenesulfamic acid. The reaction mixture turned red when the diazo solution was run into a suspension of sodium 4-toluenesulfamate, and crystallization occurred in a few minutes. The substance was recrystallized from water heated to 80° to give large, lustrous orange-red crystals; appearance of plates under the microscope.

Found %: diazo nitrogen 8.32. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

2-Nitrobenzenediazonium salt of benzenesulfamic acid. A diazo solution of maximum concentration and a thick suspension of sodium benzenesulfamate were reacted. After standing in the cold, only a small quantity of solid came down which after filtration had the form of a brown paste. Under the microscope it consisted of fine, poorly formed crystals. The paste was very easily soluble in water and imparted a yellow color. The solution coupled intensively with azo coupling agents. Due to the small quantity, the diazonium salt was not analyzed or purified.

2-Nitrobenzenediazonium salt of 4-toluenesulfamic acid. A concentrated solution of the diazo compound was run into a thick suspension of sodium 4-toluenesulfamate. The reaction mixture acquired a dark red-brown color. A small quantity of claret-colored solid came down after a few minutes. Stout, pale-red plates under the microscope.

Found %: diazo nitrogen 8.11. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

2-Methyl-4-nitrobenzenediazonium salt of benzenesulfamic acid. A precipitate came down after the cooled mixture of reactants had stood for 30 minutes. Under the microscope it consisted of stout crystals with the form of prisms with sharp ends. After recrystallization from water heated to 55°, the diazo salt acquired a claret-brown color darker than the color of 4-nitrobenzenediazonium benzenesulfamate.

Found %: diazo nitrogen 8.33. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

2-Methyl-4-nitrobenzenediazonium 4-toluenesulfamate. Mixing of the components led to formation of a reddish-violet viscous mass. The recrystallized product consisted of lustrous, dark-brown crystals with a violet tinge; stout prisms under the microscope.

Found %: diazo nitrogen 8.09. $C_{14}H_{14}O_5N_4S$. Calculated %: diazo nitrogen 8.00.

2-Chloro-4-nitrobenzenediazonium benzenesulfamate. The reaction mixture at once turned dark-brown and a chocolate-brown precipitate quickly came down and gradually became paler. This precipitate was only poorly soluble in water (yellow solution) and it did not couple intensively with azo components. Under the microscope it consisted of fine, poorly formed crystallites, altogether dissimilar from the stout crystals of the previously described diazo salts. A sample dissolved in glacial acetic acid, to which α-naphthylamine was added, gave an intense coloration. The precipitate is therefore mainly a diazoamino compound. The pure diazonium salt of benzenesulfamic acid could not be isolated from the solid. This signifies that even in a mineral acid medium, 2-chloro-4-nitrobenzenediazonium at first forms a salt with benzenesulfamic acid and the salt rapidly changes into the insoluble diazoamino compound.

2-Chloro-4-nitrobenzenediazonium 4-toluenesulfamate. The nearly black (with violet-brown tinge) reaction mixture deposited after 2–3 minutes a thick slurry of violet-black crystals with the appearance of elongated plates under the microscope. It was rapidly filtered; the product was completely soluble in water (weak-yellow color) and intensively coupled with azo components, but it could not be recrystallized or even dried without decomposition. A few minutes after it had been separated from the mother liquor and washed with glacial acetic acid, the compound began to darken and at the same time lost its solubility in water. It quickly changed into a brownish-yellow compound, insoluble in water and not coupling with azo components in a neutral medium. The new substance dissolved in glacial acetic acid with an orange color, and addition of α-naphthylamine to the solution gave a bright coloration characteristic of diazoamino compounds.

4-Chlorobenzenediazonium benzenesulfamate. A saturated solution of sodium chloride was added to the reaction mixture which was cooled with ice. Stout, golden scales came down (plates under the microscope). The product was recrystallized from water heated to 70–80°. The golden-yellow crystals were filtered, washed with iced water, pressed on porous porcelain and dried in vacuo over solid potassium hydroxide. The color of the aqueous solution of the salt varies from yellow to colorless in dependence on the concentration.

Found %: diazo nitrogen 8.95. $C_{12}H_{10}O_3N_3SCl$. Calculated %: diazo nitrogen 8.98.

4-Chlorobenzenediazonium 4-toluenesulfamate. The reaction solution turned red, and after a few minutes it deposited red crystals (stout plates under the microscope). Recrystallization gave stout, lustrous, orange-red plates. The color of the aqueous solution of the salt varied from yellow-orange to colorless in dependence on the concentration.

Found %: diazo nitrogen 8.57. $C_{13}H_{12}O_3N_3SCl$. Calculated %: diazo nitrogen 8.60.

2,5-Dichlorobenzenediazonium benzenesulfamate. After 2–3 minutes the reaction solution deposited a thick slurry of bright-red crystals. With the objective of recrystallization, the filtered precipitate was ground into a paste with 10% acetic acid solution and then dissolved in water heated to 65-70°. Stout red crystals came down after cooling, and had the appearance of needles under the microscope. The solid was washed with ether on the filter, pressed on porous porcelain and dried in vacuo. The color of the aqueous solution of the salt varied from reddish-orange to pale-yellow in dependence on the concentration.

Found %: diazo nitrogen 7.87. $C_{12}H_9O_3N_3SCl_2$. Calculated %: diazo nitrogen 8.09.

2,5-Dichlorobenzenediazonium 4-toluenesulfamate. The brown-red reaction solution gradually deposited a light-brown solid poorly soluble in water and coupling weakly with azo components. Solution of the product in glacial acetic acid, addition of α-naphthylamine and gentle heating led to development of a bright violet color. The precipitate in the main therefore consisted of the diazoamino compound.

4-Chloro-2-nitrobenzenediazonium benzenesulfamate. The reddish-brown reaction mixture crystallized after 2–3 minutes. The filtered precipitate consisted of claret-brown crystals (elongated plates under the microscope). The product was nearly completely soluble in cold water to form a pale-yellow solution, and it actively coupled with diazo components. The salt was extremely unstable. It changed partly into diazoamino compound on recrystallization or drying.

4-Chloro-2-nitrobenzenediazonium 4-toluenesulfamate. After a few minutes the reaction solution deposited a chocolate-brown substance (elongated plates under the microscope). After washing with iced water, pressing on porous porcelain and drying in vacuo, the product nearly completely retained its azo-coupling ability. On recrystallization from water it was partially converted into the diazoamino compound.

2,4,6-Tribromobenzenediazonium benzenesulfamate. After 2,4,6-tribromodiazobenzene had been run into a suspension of sodium benzenesulfamate, the reaction mixture at first was colored red-brown, but quickly lightened and deposited a yellow-brown solid which was poorly soluble in water and coupled weakly with azo components. It formed an azo dye with α-naphthylamine. The diazo salt is accordingly already converted into the diazoamino compound in the mineral acid reaction solution.

2,4,6-Tribromobenzenediazonium 4-toluenesulfamate. The reaction mixture acquired an orange-brown color when a concentrated diazo solution was run into the thick suspension of toluenesulfamate. A small precipitate came down after a few minutes. The quantity was not increased by salting-out and cooling. The orange-yellow, filtered product only dissolved partly in water and coupled weakly with azo components. Two forms of crystals were observed under the microscope: small but well-formed plates (probably diazo salt) and very fine crystallites of indeterminate structure, sticking to the plates. The pure diazo salt could not be isolated from the precipitate.

Benzenediazonium chloride and sodium benzenesulfamate. A yellow solution was formed when a solution of benzenediazonium chloride of maximum concentration was run into a thick suspension of sodium benzenesulfamate. No precipitate could be obtained by cooling, by salting-out with sodium chloride or sodium sulfate, etc.

4-Toluenediazonium chloride, 4-methoxybenzenediazonium chloride and 5-chlorobenzenediazonium chloride form yellow to orange solutions with sodium benzenesulfamate from which no precipitate could be obtained. Similar results were obtained with benzenediazonium chloride and 4-toluenediazonium chloride on the one hand and sodium toluenesulfamate on the other.

Measurement of the absorption spectra of aqueous solutions of aryldiazonium sulfamates. Saturated aqueous solutions of the following diazo salts were prepared: a) 0.07757 M 4-nitrobenzenediazonium benzenesulfamate; b) 0.08903 M 4-nitrobenzenediazonium 4-toluenesulfamate; c) 0.2406 M 4-chlorobenzenediazonium benzenesulfamate; d) 0.1279 M 4-chlorobenzenediazonium benzenesulfamate.

Each of the saturated solutions was diluted 4-fold and 10-fold with water. The absorption spectra of the solutions were measured with the SF-4 spectrophotometer. The optical density D was determined at wavelengths of 700 to 380–280 mμ. The molecular coefficient of absorption was calculated from the formula

$$\varepsilon = \frac{1}{B \cdot C} \cdot 2.3\,D,$$

where B is the thickness of the solution layer in centimeters and C is the molar concentration per liter. Aqueous solutions of aryldiazonium sulfamates have poor stability. Solutions must therefore be frequently replaced by fresh ones during the measurements.

SUMMARY

1. Deeply colored salts ranging in color from yellow and orange to nearly black are formed by reaction of arylsulfamic acids with aryldiazonium compounds containing electron-accepting substituents.

2. It was shown that the more electronegative the substituents in the aryldiazonium cation are the deeper the color of the resulting salt of arylsulfamic acid will be. Such an effect is induced by electron-donating substituents in the arylsulfamic acid.

3. In water the aryldiazonium sulfamates form saturated solutions that are very much more colored than the solid salts. They lose their color on dilution and accordingly do not obey the Lambert-Beer law.

4. It was shown that the color characteristics of aryldiazonium sulfamates are caused by the formation of undissociated salts by these components. The loss of color of aqueous solutions of aryldiazonium sulfamates on dilution is a consequence of their dissociation into colorless cations and anions.

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Received March 30, 1957

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*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS ON THIOSULFONIC ACIDS

III. ALKYL ESTERS OF PHENYLMETHANE THIOSULFONIC ACID AND THEIR ANTIBACTERIAL PROPERTIES

B. G. Boldyrev and Iu. I. Kofman

In the preceding communications [1,2] on the properties of alkyl esters (I) of alkanethiosulfonic acids obtained by one of us with co-workers, we observed that the antibacterial activity of these compounds does not depend upon the size and structure of the radicals on the side of the oxide sulfur and substantially remains constant for esters of thiosulfonic acids of both normal and isostructures with 1 to 4 carbon atoms.

$$\underset{(I)}{Alk-SO_2-S-Alk'} \quad \underset{(II)}{C_6H_5-CH_2-SO_2-S-Alk}$$

For this reason we decided in the present work to synthesize and study the properties of alkyl esters (II) of phenylmethanethiosulfonic acid in order to establish the influence of change of character of the radicals of thiosulfonic acids on the antibacterial activity of the esters.

We synthesized alkyl esters of phenylmethanethiosulfonic acid by our previously described method [1]; the esters prepared are listed in the table. They are colorless, crystalline substances with a weak specific odor, readily soluble in alcohol, ether, acetone and other organic solvents, poorly soluble in water.

TABLE

Alkyl Esters of Phenylmethanethiosulfonic Acid

$$C_6H_5-CH_2-SO_2-S-Alk$$

Preparation no.	Alk	Melting point	Sulfur content (%)		Yield (%)	Crystal forms (from anhydrous alcohol)
			found	calc.		
1	CH_3-CH_2-	70—71°	29.88	29.80	29.3	Tetragonal prisms
2	$CH_3-CH_2-CH_2-$ . . .	44	28.02	27.84	44.4	Hexagonal prisms
3	$\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!>CH-$	61—62	27.74	27.84	21.0	Elongated hexagonal prisms
4	$CH_2=CH-CH_2-$ . . .	27	27.95, 28.02	28.09	33.8	From 40% alcohol: crystals of indeterminate form
5	$CH_3-CH_2-CH_2-CH_2-$	34—35	26.17	26.24	37.0	Elongated thin needles
6	$\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!>CH-CH_2-$ . . .	44—45	26.10, 26.30	26.24	22.0	Elongated thin needles

A study of the antibacterial properties of the esters (II), carried out by the Institute of Microbiology of the Academy of Sciences of the Ukrainian SSR, showed that the activity of these compounds towards gram-positive, gram-negative and acid-resistant bacteria is lower than that of alkyl esters of alkanethiosulfonic acids containing 1 to 4 carbon atoms; at the same time the activity of esters (II) towards various fungi increases to a considerable degree.

The present work thus showed that the antibacterial properties of esters of thiosulfonic acids depend not only on the character of the radicals linked to the sulfide sulfur but also on the structure of the original thiosulfonic acids.

EXPERIMENTAL

The intermediates for synthesis of esters (II)—sodium phenylmethanesulfonate and phenylmethanesulfochloride—were prepared by the literature methods [3,4].

Potassium phenylmethanethiosulfonate, not previously described, was synthesized in a similar manner to other alkanethiosulfonates [1,2]. It is a colorless, crystalline substance with m.p. 220–221°, readily soluble in water, more difficultly soluble in boiling alcohols, insoluble in ether, acetone, benzene and other organic solvents. The potassium salt crystallizes from ethyl alcohol in the form of slender, rectangular plates; from butyl alcohol it crystallizes as extremely thin, square crystals.

Found %: S 28.16. $C_7H_7O_2S_2K$. Calculated %: S 28.33.

Alkyl esters of phenylmethanethiosulfonic acid were prepared as in the preceding papers [1,2]. They were usually isolated in the form of colored, oily liquids which crystallized with difficulty in a freezing mixture and required numerous recrystallizations from 40% alcohol; this also accounts for the low yields of pure products. The quantity of acetone influences the purity of the end products; when used in the proportion of less than 100 ml per 20 g of thiosulfonate, the products are more strongly colored. Removal of acetone from the reaction mass was effected by suction at room temperature in vacuo, since evaporation on a water bath led to more deeply colored and very difficultly crystallizable products.

SUMMARY

1. Potassium phenylmethanethiosulfonate and 6 alkyl esters of phenylmethanethiosulfonic acid, not previously described, were synthesized.

2. The antibacterial properties of esters of phenylmethanethiosulfonic acid were studied; data for these compounds showed that the antibacterial activity of esters of thiosulfonic acids depends not only on the character of the radicals attached to the sulfide sulfur but also on the structure of the original thiosulfonic acids.

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Received February 4, 1957

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*Original Russian pagination. See C. B. Translation.

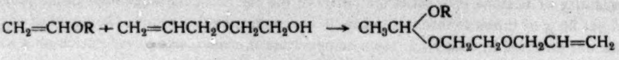
THE REACTION OF ALLYLOXYETHANOL WITH VINYL ETHERS

V. N. Kotrelev and I. K. Rubtsova

The investigations carried out by M. F. Shostakovskii et al. [1] on a large number of individual syntheses demonstrated the possibility of preparing acetals by reacting vinyl ethers with hydroxyl-containing compounds. In particular, they described the synthesis of acetals containing an unsaturated radical [2].

The present investigation was undertaken to prepare acetals based on allyloxyethanol and to examine their capacity for copolymerization.

These acetals were synthesized by M. F. Shostakovskii's method [1] from vinyl ethers and allyloxyethanol.



$$CH_2{=}CHOR + CH_2{=}CHCH_2OCH_2CH_2OH \longrightarrow CH_3CH\begin{cases}OR\\OCH_2CH_2OCH_2CH{=}CH_2\end{cases}$$

where: $R = C_2H_5$, iso-C_3H_7, n-C_4H_9.

It is known [3] that the acetals of allyl alcohol (diallylformal, ethylal, butyral) are incapable of polymerization by a radical or ionic mechanism, but readily form copolymers with a lattice structure with polar monomers (vinyl acetate, acrylates, etc.).

We investigated the capacity of allyloxyethanol acetals for copolymerization with methyl methacrylate in a ratio of 10 : 90 in the presence of benzoyl peroxide. In all cases solid, colorless, transparent polymers were obtained; some of them had a higher thermostability than poly-(methyl methacrylate).

EXPERIMENTAL

As starting materials we used allyloxyethanol, prepared by the method we developed previously [4], and vinyl ethers, which were kindly given to us by M. F. Shostakovskii. The constants of the starting materials corresponded to literature data [1].

On distilling the acetals obtained as a result of disproportionation, we obtained three main fractions: 1st fraction—the symmetrical, low-boiling acetal, which corresponded to literature data [2] in its constants; 2nd—the unsymmetrical acetal and the 3rd fraction was the same in all cases and consisted of diallyloxyethyl acetal. The constants and the analysis results of the acetals obtained are given in Table 1.

Ethyl allyloxyethyl acetal. 36 g of vinyl ethyl ether and 51 g of allyloxyethanol were used. We obtained 15.4 g of diethyl acetal (b.p. 102–104°), 59.8 g of ethyl allyloxyethyl acetal and 7.6 g of diallyloxyethyl acetal.

Isopropyl allyloxyethyl acetal. 27.7 g of vinyl isopropyl ether and 32.8 g of allyloxyethanol were used. We obtained 8.2 g of diisopropyl acetal (b.p. 45–46° at 15 mm), 35.5 g of isopropyl allyloxyethyl acetal and 13.62 g of diallyloxyethyl acetal.

n-Butyl allyloxyethyl acetal. 18.3 g of vinyl n-butyl ether and 18.4 g of allyloxyethanol were used. We obtained 6.3 g of dibutyl acetal (b.p. 184–186°), 14.2 g of butyl allyloxyethyl acetal and 7.6 g of diallyloxyethyl acetal.

TABLE 1

Allyloxyethanol Acetals of the Type $CH_3CH{<}\begin{matrix}OR\\ OCH_2CH_2OCH_2CH{=}CH_2\end{matrix}$

Name of acetal	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		% C		% H		M	
				found	calc.	found	calc.	found	calc.	found	calc.
Ethyl allyloxyethyl acetal	82— 83° (15)	0.9146	1.4163	48.0	48.22	61.10, 62.19	62.0	10.31, 10.35	10.40	171.2, 170.6	174
Isopropyl allyloxyethyl acetal	87— 89° (15)	0.9013	1.4192	52.77	52.84	63.69, 63.71	63.80	10.54, 10.51	10.63	186.3, 185.1	188
n-Butyl allyloxyethyl acetal	110—112° (18)	0.9022	1.4257	57.42	57.47	65.13, 65.16	65.34	10.80, 10.88	10.83	199.8, 197.9	202
Diallyloxyethyl acetal	96— 98° (2)	0.9615	1.4410	63.25	63.24	62.49, 62.54	62.6	9.51, 9.53	9.56	225.2, 226.6	230

TABLE 2

Copolymers of Allyloxyethanol Acetals with Methyl Methacrylate

Name of starting acetal	Properties of copolymers	
	Brinell hardness (in kg/mm²)	VIK thermostability
Ethyl allyloxyethyl acetal	11.37	78–79°
Isopropyl allyloxyethyl acetal	12.25	80–81
n-Butyl allyloxyethyl acetal	13.27	84–86
Diallyloxyethyl acetal	15.25	110–112

Copolymerization of acetals obtained with methyl methacrylate. The copolymerization was performed with the proportions 90% of methyl methacrylate and 10% of each of the acetals. The initiator was benzoyl peroxide (1% of the weight of the mixture). In all the experiments the temperature was gradually raised from 45 to 100° by 10° over equal time intervals. After 72 hours we obtained clear, colorless, solid polymers. The properties of some of them are given in Table 2.

SUMMARY

1. The previously unknown ethyl allyloxyethyl acetal, isopropyl ethylallyloxyethyl acetal, n-butyl allyloxyethyl acetal and diallyloxyethyl acetal of acetaldehyde were prepared and described.

2. Copolymerization of the acetals prepared with methyl methacrylate gave copolymers which had a higher thermostability than that of poly-(methyl methacrylate).

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Received February 14, 1957

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* In Russian.

THE SYNTHESIS OF PHENYLDIFLUOROACETIC ACID AND ITS DERIVATIVES

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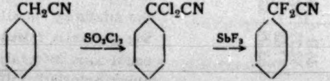
The derivatives of phenylacetic acid have been studied thoroughly as many of them are physiologically active substances with a capacity for stimulating the growth of plants [1].

We undertook the synthesis of phenyldifluoroacetic acid and its derivatives which have not been described in the literature. For this purpose we studied the reaction of phenyldichloroacetonitrile with antimony trifluoride.

As the starting material we used benzyl cyanide which was chlorinated by Claisen's method [2] with sulfuryl chloride and then fluorinated with antimony trifluoride. It was found that the cyano group was untouched and was not substituted by fluorine. The reaction proceeded by the scheme



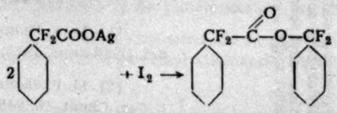
The nitrile obtained was converted to the amide in the cold by concentrated sulfuric acid. When the amide was heated with 10% sodium hydroxide it gave phenyldifluoroacetic acid.

Nitration of this acid gave m-nitrophenyldifluoroacetic acid. The position of the nitro group was determined by heating the m-nitrophenyldifluoroacetic acid in sulfuric acid (monohydrate). This gave m-nitrobenzoic acid.

Phenyldifluoroacetic and m-nitrophenyldifluoroacetic acids are quite strong acids. Their pK* values equal 2.16 and 1.89, respectively.

Reduction of m-nitrophenyldifluoroacetic acid gave the m-amino derivative. Apparently, m-aminophenyldifluoroacetic acid is an internal salt. It melted with decomposition at 235–240°, crystallized from water, was insoluble in organic solvents and soluble in solutions of soda and alkali and dissolved with difficulty in acids. m-Aminophenyldifluoroacetic acid was diazotized to give addition products.

The silver salt of phenyldifluoroacetic acid reacted peculiarly with iodine to form the ω,ω-difluorobenzyl ester of phenyldifluoroacetic acid by the scheme



The structure of the ester obtained was determined by hydrolyzing it in an acid and an alkaline medium. When heated with sulfuric acid (monohydrate) it formed benzoic acid quantitatively; when boiled with 10% sodium hydroxide it gave a mixture of benzoic and phenyldifluoroacetic acids.

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* The pK was determined by potentiometric titration using a tube pH meter with a glass electrode.

We tried to alter the direction of the reaction of the silver salt of phenyldifluoroacetic acid with iodine to obtain phenyldifluoroiodomethane. For this purpose the reaction was carried out by grinding the dry components in the cold in equimolecular amounts or by heating iodine with the silver salt of phenyldifluoroacetic acid in carbon tetrachloride. The ratio of iodine to silver salt, the order of addition and the concentration of iodine in the carbon tetrachloride solution were varied. However, in all cases only ω,ω-difluorobenzyl ester of phenyldifluoroacetic acid was isolated.

EXPERIMENTAL

Phenyldichloroacetonitrile. 58 g of benzyl cyanide and 332 g of sulfuryl chloride were mixed. When the mixture had stood for a day, the excess sulfuryl chloride was distilled off at room temperature and the product vacuum distilled. The yield was 74 g (89.8%). The b.p. was 91–92° (8 mm). The product had a lachrimatory effect. A b.p. of 135° (20 mm) is reported in the literature [2].

Phenyldifluoroacetamide. 30 g of phenyldichloroacetonitrile and 34.6 g of antimony trifluoride were heated over a naked flame until a reaction began. The reaction proceeded for some time without heating. On further heating, a clear, colorless liquid distilled off at 150–160°. The product was dissolved in ether and the ether solution washed with dilute hydrochloric acid to remove antimony trichloride and then with water and dried. The ether was removed and the nitrile distilled from a flask with a pear fractionating column. A fraction was collected from 151–153°. The product was redistilled. The b.p. was 151–152°. The yield was 10 g (42%).

5 g of phenyldifluoroacetonitrile was mixed with 20 g of concentrated sulfuric acid and left overnight. The clear, colorless solution was poured onto ice. The white precipitate of amide formed was recrystallized from hot water. The yield was 4.65 g (83%) and the m.p. 114–115°.

Found %: N 8.17; F 22.05. $C_8H_7ONF_2$. Calculated %: N 8.18; F 22.22.

Phenyldifluoroacetic acid. 14.5 g of phenyldifluoroacetamide was boiled for 12 hours with 41.5 ml of 10% sodium hydroxide under reflux in a round-bottomed flask. The hydrolyzate was acidified with dilute sulfuric acid. The phenyldifluoroacetic acid precipitated as an oil. The acid was extracted with ether, the ether solution dried and the ether distilled off. The solid, crude product was recrystallized from petroleum ether (b.p. 47–50°). The yield was 12 g (82.2%). The m.p. was 76–77°. The substance formed clear, colorless needles. The acid was readily soluble in benzene, ether and methyl and ethyl alcohols.

Found %: F 21.97. $C_8H_6O_2F_2$. Calculated %: F 22.09.

Phenyldifluoroacetyl chloride. 4 g of phenyldifluoroacetic acid was boiled with 15 ml of thionyl chloride for 6 hours. The excess thionyl chloride was distilled off. The residue was vacuum distilled. The yield was 3.7 g (84%). The colorless oil had b.p. 67–68° (15 mm).

Ethyl phenyldifluoroacetate. 2.5 g of phenyldifluoroacetyl chloride was carefully added to 3 g of anhydrous ethyl alcohol. Heat was evolved during the reaction.

To complete the reaction the mixture was boiled under reflux for 30 minutes on a water bath. The excess alcohol was distilled off on a water bath and the residue vacuum distilled. The yield was 1.6 g (61.5%) and the b.p. 88–89° (9 mm). The colorless oil had a pleasant smell.

Phenyldifluoroacetanilide. Phenyldifluoroacetyl chloride was mixed with a solution of aniline in dry benzene in the cold. The yield of anilide was quantitative. The m.p. was 106–107° (from aqueous alcohol).

Found %: N 5.78. $C_{14}H_{11}ONF_2$. Calculated %: N 5.66.

m-Nitrophenyldifluoroacetic acid. Into a three-necked flask fitted with a thermometer and a stirrer was placed 3.5 ml of nitric acid (d 1.5) and 5.9 ml of sulfuric acid (d 1.83). The mixture was cooled to 0° and 4 g of phenyldifluoroacetic acid was added in portions with stirring. The temperature of the reaction mixture was kept at 20–22° and the acid added over a period of 35 minutes. The mixture was left for 1 hour at room temperature (17°) and then for another hour at 40–45°. When the reaction mixture was poured onto ice, a white crystalline precipitate formed. The precipitate was filtered off, washed with ice-water and dried. The product was recrystallized from benzene. The yield was 3.93 g (78.6%). The m.p. was 113–114°.

Found %: N 6.47. $C_8H_5O_4NF_2$. Calculated %: N 6.45.

m-Aminophenyldifluoroacetic acid. Into a reaction vessel fitted with a stirrer, a thermometer and a reflux condenser was placed 1.5 g of m-nitrophenyldifluoroacetic acid, 1.7 ml of concentrated hydrochloric acid and 1.7 ml of water. The contents of the reaction vessel were heated to 60° on a water bath and stirred. 1.5 g of iron filings was added in small portions while the temperature was gradually raised to 80°. The temperature was kept at 80° for 2 hours and then the solution was made weakly alkaline to phenolphthalein with 10% sodium hydroxide solution and filtered. The sludge was washed with a 10% sodium hydroxide solution and water. The filtrate was acidified with hydrochloric acid and evaporated on a water bath until crystallization began. The product was readily soluble in alkali and quantitatively precipitated by hydrochloric and acetic acids. It crystallized from hot water in the form of lustrous needles. The decomp. point was 235-240°. The yield was 1 g (77.5%).

Found %: F 20.17; N 7.49. $C_8H_7O_2NF_2$. Calculated %: F 20.3; N 7.48.

Silver salt of phenyldifluoroacetic acid. A solution of 5.8 g of the sodium salt of phenyldifluoroacetic acid in 20 ml of water was mixed with 5 g of silver nitrate in 10 ml of water. The salt precipitated was recrystallized from hot water. The decomp. point was 205°. The yield was 6.5 g (81.3%).

Found %: Ag 38.5. $C_8H_5O_2F_2Ag$. Calculated %: Ag 38.6.

ω,ω-Difluorobenzyl ester of phenyldifluoroacetic acid. 5.7 g of the dry silver salt and 5.7 g of ground iodine were placed in a round-bottomed flask fitted with a reflux condenser, and 25 ml of anhydrous carbon tetrachloride added. The mixture was placed on a paraffin bath and heated to 65°. At 67° a vigorous reaction began and proceeded for 10 minutes without external heating. The temperature of the bath was maintained at 67–70° for 20 minutes and then raised until the carbon tetrachloride boiled gently for 1 hour. The precipitate of silver iodide was filtered off and washed with carbon tetrachloride. The filtrate was washed free from iodine by titration with 0.1 N sodium bisulfite solution and dried. The carbon tetrachloride was distilled off on a water bath under reduced pressure provided by a water pump. A crystalline product remained. The yield was 2.7 g (90%). The clear, colorless prisms had m.p. 65.5–66° (from petroleum ether).

Found %: F 25.24. $C_{15}H_{10}O_2F_2$. Calculated %: F 25.5.

SUMMARY

The synthesis of phenyldifluoroacetic acid and its derivatives (nitrile, amide, acid chloride, ethyl ester and anilide) are described.

We prepared m-nitro- and m-aminophenyldifluoroacetic acids.

It was shown that the silver salt of phenyldifluoroacetic acid reacts with iodine to form the ω,ω-difluorobenzyl ester of phenyldifluoroacetic acid.

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Received February 21, 1957

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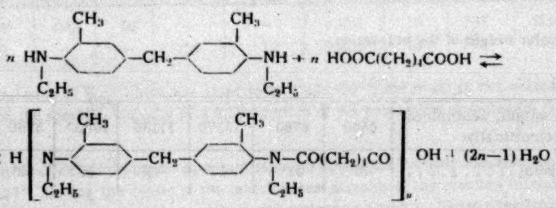
* In Russian.

SYNTHESIS AND INVESTIGATION OF POLY-3,3'-DIMETHYL-DIPHENYLMETHANEADIPO-N,N'-DIETHYLAMIDE

O. Ia. Fedotova, M. A. Askarov and L. N. Sedov

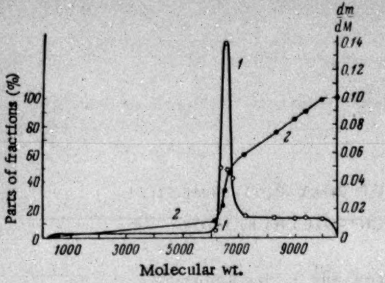
In one of our earlier papers [1] we examined some of the characteristics of the synthesis and properties of poly-3,3'-dimethyldiphenylmethaneadipamide. It was noted that this product is very hard, high-melting and insoluble in the usual organic solvents. Wishing to study the effect of substitution on the nitrogen and to obtain polymers soluble in ordinary solvents, in the present work we turned our attention to one of the most widely used methods of modifying polyamides, namely to the use of N-alkylated diamines. For this purpose N,N'-diethyl-4,4'-diamino-3,3'-dimethyldiphenylmethane [2], which reacts with adipic acid in the following way, was taken:



From this polycondensation a low-melting, brittle, glass-like product was obtained, of pale yellow color, soluble in the lower alcohols, acetone, benzene, formic and acetic acids, tricresol etc. The specific viscosity of a 0.5% solution of the polyamide in methanol was 0.09–0.13, which, with $K_m = 10.45 \cdot 10^{-4}$, corresponds to molecular weights of 9,000–12,000. We determined the value of K_m used by the light-scattering method; a similar result (K_m $10.75 \cdot 10^{-4}$) was obtained by chemical determination of end groups.

A series of experiments enabled us to determine the optimum conditions for the synthesis of the polyamide, which in general outline was as follows: the highest molecular weight polymer is obtained by carrying out the reaction in a stream of inert gas for 5 hours and then in vacuum (3–5 mm) at 240–260°. The use of vacuum for completing the reaction enables the molecular weight of the polyamide to be increased from 5,500–6,500 to 9,050–9,330.

It is known that aromatic diamines in contrast to diamines of the aliphatic series do not give salts with dicarboxylic acids [3]; this hinders to a marked extent the maintenance of the equimolecular relationship of the initial substances during the polycondensation process because of the different volatility of the components. In the course of the work it was established that disturbance of the equimolecular relationship of the initial substances took place because of the volatility of the diamine. As is known, a change in diamine concentration during the reaction process leads to lowering of the molecular weight as a result of acidolysis [4]. With the object of obtaining a polyamide of higher molecular weight the effect was studied of excess diamine (0.5 to 10% above equimolecular) on the molecular weight and melting point of the polyamide formed. It was shown that a 2% excess of diamine in the polycondensation in both the fusion and solvent processes can raise the molecular weight of the polyamide from 8,500–8,780 to 11,130–12,000, and the melting point from 46 to 78°.



Differential and integral molecular weight distribution curves. 1) Differential curve, 2) integral curve.

It is known that polyamides possess little polydispersity in molecular weight because of intensive interchange processes between the molecules of the polymers, monomers and low-molecular reaction products. This fact was demonstrated by V. V. Korshak and V. A. Zamiatina [5] by the fractionation method and by S. E. Bresler et al. [6] by the method of sedimentation in the ultracentrifuge. Our investigation of the molecular weight distribution of the polyamide indicated a high degree of monodispersity for poly-3,3'-dimethyldiphenylmethaneadipo-N,N'-diethylamide. About 50% of the polymer has molecular weights within the narrow range of 6,000 to 7,000. Integral and differential molecular weight distribution curves are shown in the diagram.

Examination of the melting-point and molecular-weight data (Table 1) of the polyamide obtained allows the conclusion to be drawn that there is a linear relationship between them.

The equation which expresses this relationship analytically was derived graphically; this equation has the following form:

$$T_{\text{m.p.}} = \frac{M - 4000}{96.2},$$

where M is the molecular weight of the polyamide.

TABLE 1

Molecular weight, determined viscometrically	8500	8780	10370	11130	10550	8780	8500
Melting point.	46°	52°	65°	78°	65°	52°	47°

In order to verify the relationship found, a number of samples of poly-3,3'-dimethyldiphenylmethaneadipo-N,N'-diethylamide were specially prepared and their melting points and viscometric molecular weights determined. Comparison of these molecular weights with the molecular weight figures calculated from the melting points confirms the correctness of the relationship established (Table 2).

TABLE 2

Melting point	Molecular weight		Relative error (in percent)
	determined viscometrically	calculated from the melting point	
38°	7560	7650	1.2
75	11360	11215	0.9
76	11360	11310	0.1
79	11600	11600	0.0

For the purpose of studying the possibility of obtaining a polyamide of higher molecular weight we set up a series of catalyzed polycondensation experiments. It is known [3] that phosphoric acid acts as a catalyst in the process of polyamide formation. In the present work another side of this question was investigated, namely the effect of phosphoric acid on the molecular weight of the polyamide. It was discovered that addition of 0.3–2.1% of phosphoric acid causes a relative lowering of molecular weight of approximately 4,000–2,000. The addition of 3% or more of phosphoric acid does not affect the molecular weight of the polyamide. At increased temperatures (265-275°) in the presence of phosphoric acid, infusible and insoluble polymers were formed, evidently in consequence of cross-linking between separate polyamide chains.

EXPERIMENTAL

The synthesis of poly-3,3'-dimethyldiphenylmethaneadipo-N,N'-diethylamide was carried out by heating mixtures of N,N'-diethyl-4,4'-diamino-3,3'-dimethyldiphenylmethane and adipic acid in a three-necked flask or in special equipment, on a Wood's metal bath in a current of CO_2. Before determining the molecular weight the polymer was broken up and freed from monomer residues by heating in a 10% aqueous methanol solution.

For determining the magnitude of K_m of methanol solutions of the polyamide under investigation, the method of chemical determination of end groups was used. For this purpose polyamides of low degrees of polycondensation were specially prepared and the acid and amine numbers of the initial monomer mixture (AN_0 and AmN_0) and of the end product (AN and AmN) were determined. On the basis of the experimental results the degree of conversion of monomers to polymer (p), the degree of polycondensation (n) and the molecular weight (M) were calculated. The following relationships were used in the calculations:

$$p = \frac{AmN_0 - AmN}{AmN_0}; \quad p = \frac{AN_0 - AN}{AN_0}; \quad n = \frac{1}{1-p}; \quad M = M_0 + 18,$$

where M_0 is the molecular weight of the elementary chain segment. The results are given in Table 3.

TABLE 3

Weight of sample (in g)	AN_0	AN	AmN_0	AmN	p	n	M_0	M
1.3370	262	20	–	–	0.923	13	392	5114
1.5961	—	—	170	12	0.928	14	392	5506

For the calculation of K_m, which was found to be $10.75 \cdot 10^{-4}$, the mean of two molecular weight determinations and the specific viscosity of a 0.5% solution of the polyamide in methanol ($\eta_{spec.}$ 0.058) were used.

With the object of determining the optimum reaction conditions the polycondensation was carried out at 220 and 250–255°. During the course of the reaction, test samples of the reaction mixture were removed for determination of their acid and amine numbers and molecular weights. These experiments showed that the reaction proceeded to the greatest extent in the first hour. There is no advantage in heating for more than 5 hours because in the first 2–3 hours the molecular weight rises to 3,000–5,000 (depending on the reaction temperature) and the acid number falls from 262 to 35.0; during the next 2 hours the molecular weight rises only to 5,000–5,500. When vacuum treatment is included a new, sharp rise in molecular weight to approximately 7,000–9,000 is observed. Increasing the reaction time in vacuo beyond 2 hours is also of no advantage since the increase in molecular weight again ceases.

In the study of the effect of reaction temperature on the properties of the polyamide (molecular weight, acid and amine number) experiments at 140 and 260° were carried out under the conditions described above. The results are given in Table 4.

TABLE 4

Properties of polyamide	Reaction temperature							Initial values
	140°	160°	180°	200°	220°	240°	260°	
Molecular weight determined viscometrically (K_m $10.45 \cdot 10^{-4}$). . . .	1790	3110	5000	6200	8470	9050	9330	–
Amine number	62.1	49.2	44.5	39.5	24.8	20.2	16.2	170
Acid number	74.2	69.3	64.5	60.0	45.0	31.7	27.0	262

For the study of polydispersity a weighed sample of the polyamide (50.2 g) was dissolved in 1200 ml of methyl alcohol; fractionation was carried out by the method of fractional precipitation of the polyamide with distilled water from a 0.5% solution of the polymer. The weight and molecular weight (viscometric) of each sample separated was determined after drying in a vacuum desiccator. Integral and differential molecular weight distribution curves were constructed from the results obtained.

SUMMARY

1. Poly-3,3'-dimethyldiphenylmethaneadipo-N,N'-diethylamide, which is soluble in ordinary organic solvents, has been synthesized for the first time. The effect of N-substitution on the properties of the polymer has been determined. The optimum conditions of preparation have been found.

2. The value of K_m for alcoholic solutions of the polyamide was found to be $10.75 \cdot 10^{-4}$.

3. Differential and integral molecular-weight distribution curves of the polyamide have been constructed, a low degree of polydispersity being found.

4. An equation has been derived connecting the melting point of poly-3,3'-dimethyldiphenylmethane-adipo-N,N'-diethylamide with its molecular weight.

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Received May 9, 1957

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*Original Russian pagination. See C. B. Translation.

**In Russian.

THE SYNTHESIS OF N-SUBSTITUTED METHACRYLAMIDES

IV. ACYLATION OF AROMATIC AMINES WITH METHACRYLYL CHLORIDE IN AN AQUEOUS MEDIUM

T. A. Sokolova and L. A. Ovsiannikova

The difference observed between the hydrolysis rate of methacrylyl chloride and its reaction rate with aromatic amines made it possible for us to conduct the acylation of amines in an aqueous medium. Previously, N-arylmethacrylamides were prepared in an organic solvent medium [1,2].

As the experiments showed, N-arylmethacrylamides may be prepared in good yields by adding 1 mole of methacrylyl chloride to an emulsion or a suspension of 2 moles of aromatic amine in water with vigorous stirring. In this case the water served as a diluent. The second mole of amine combined with the hydrogen chloride molecule evolved during the reaction and passed into the aqueous solution in the form of the hydrochloride. The N-arylmethacrylamide separated either as a liquid layer or in the solid state and could be isolated by filtration or extraction. The reaction products obtained were only slightly colored and had definite melting points. The dried products were further purified by recrystallization or distillation under reduced pressure.

N-Arylmethacrylamides

Name of monomer	Yield of crude product (in %)	Melting point	
		crude product	pure product
m-Fluorophenylmethacrylamide	87.5	71.5–72°	73–73.5°
p-Fluorophenylmethacrylamide	69	70.5–71	73–73.5
p-Iodophenylmethacrylamide	75	135–135.5	137.5–138
m-Methoxyphenylmethacrylamide	92	79–81	92.5–93
p-Dimethylaminophenylmethacrylamide	90	129.5–131	131–131.5
o-Methoxyphenylmethacrylamide	89.8	liquid	b.p. 141° at 2 mm
o-Ethoxyphenylmethacrylamide	89.0	40–40.5	44.5–45
m-Ethoxyphenylmethacrylamide	68	94–95	95.5–96
Phenylmethacrylamide	84.5	83.5–84.5	85–85.5
o-Tolylmethacrylamide	72.8	92.5–93	94.5–95
m-Chlorophenylmethacrylamide	82.4	103.5–104.5	105–105.5
p-Chlorophenylmethacrylamide	80.5	110.5–111.5	112–112.5
p-Methoxyphenylmethacrylamide	77.5	88–89	90.5–91
p-Tolylmethacrylamide	84.5	85–86	88.5–89

The experimental results on the preparation of N-arylmethacrylamides in an aqueous medium are given in the table. The melting point of the reaction products are corrected.

The acylation may also be carried out by substituting 1 mole of the starting amine by 1 mole of dimethylaniline, which does not react with methacrylyl chloride and is a substance which combines with hydrogen chloride. The product yields did not decrease as a result of this substitution.

The yield of N-arylmethacrylamide was almost half the amount when equimolecular amounts of the reagents were used. 1 mole of amine per mole of methacrylyl chloride was sufficient only in the preparation of p-dimethylaminophenylmethacrylamide, as the starting p-dimethylphenylenediamine was itself capable of combining with the hydrogen chloride through its dimethylamino group.

In the case of acylation of solid amines which were insoluble in water, it was advantageous to grind them well first. Using this method we were able to obtain a good yield of o-ethoxyphenylmethacrylamide which was prepared in the form of a polymer when the reaction was carried out in an organic solvent medium [2]. Previously, this monomer has been obtained only via an organomagnesium compound [3].

The method developed however, cannot be applied to the preparation of N-arylmethacrylamides from amines of such low basicity as diphenylamines ($K^{15}_{bas.}$ $7.60 \cdot 10^{-14}$) [4], apparently due to the low rate of acylation of this amine with methacrylyl chloride.

EXPERIMENTAL*

Preparation of N-arylmethacrylamides. 0.4 mole of the aromatic amine was stirred with 100 ml of water in a two-necked, round-bottomed flask, fitted with a stirrer and a dropping funnel. With very vigorous stirring, 0.2 mole of methacrylyl chloride was added dropwise over a period of about 2 hours to the emulsion or suspension of the amine in water. At the end of the addition the mass was acidified with hydrochloric acid until Congo paper gave a blue color and stirred for another half hour, and then the solid N-substituted methacrylamide produced was filtered off, washed with water until neutral and dried at 45–60°. If the reaction product was a liquid, the oily layer which separated was extracted with ether. The extract was dried with anhydrous magnesium sulfate, the ether distilled off and the residue distilled under reduced pressure. The crude product was purified either by recrystallization or redistillation in vacuum.

Preparation of N-p-dimethylaminophenylmethacrylamide. After adding the methacrylyl chloride, we obtained a solution, from which the product was isolated by the addition of alkali until paper soaked in brilliant yellow gave a pale red color. The precipitate of p-dimethylaminophenylmethacrylamide formed was filtered off and then treated as described above.

Properties of new N-arylmethacrylamides

m-Fluorophenylmethacrylamide formed white crystals, which were soluble in acetone, benzene, alcohol, methyl methacrylate and chloroform in the cold and insoluble in water.

Found %: N 7.90; F 10.64. $C_{10}H_{10}ONF$. Calculated %: N 7.71; F 10.61.

p-Fluorophenylmethacrylamide was a white crystalline substance, soluble in acetone, benzene, methyl methacrylate and chloroform in the cold and insoluble in water.

Found %: F 10.53. $C_{10}H_{10}ONF$. Calculated %: F 10.61.

p-Iodophenylmethacrylamide formed fine, white crystals which were soluble in acetone, benzene, alcohol and chloroform and insoluble in water.

Found %: C 41.83; H 3.52; N 4.83; I 44.45. $C_{10}H_{10}ONI$. Calculated %: C 41.81; H 3.49; N 4.87; I 44.25.

m-Methoxyphenylmethacrylamide gave white crystals, which were soluble in acetone, alcohol, benzene and chloroform in the cold and insoluble in water.

Found %: C 69.36; H 6.96; N 7.74. $C_{11}H_{13}O_2N$. Calculated %: C 69.11; H 6.81; N 7.33.

p-Dimethylaminophenylmethacrylamide crystallized from alcohol as yellow prisms. They were soluble in acetone, chloroform and methyl methacrylate in the cold; dissolved in alcohol and benzene on heating and were insoluble in water.

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* With the assistance of A. M. Kashnitskaia.

Found %: C 70.55; H 7.98; N 13.78. $C_{12}H_{16}ON_2$. **Calculated %:** C 70.59; H 7.84; N 13.72.

SUMMARY

1. A method was developed for preparing N-arylmethacrylamides in an aqueous medium, which makes it possible to obtain even readily polymerizable monomers (such as o-ethoxyphenylmethacrylamide). The method was tested by the acylation of 14 aromatic amines with $K_{bas.}$ of the order of $10^{-9}-10^{-11}$.

2. Five new N-arylmethacrylamides were obtained: p-iodo-, m-fluoro-, p-fluoro-, m-methoxy- and p-dimethylamino-phenylmethacrylamides.

3. It was shown that the method found was unsuitable for the acylation of amines of low basicity, $K_{bas.}$ of the order of 10^{-14}, (such as diphenylamine) using methacrylyl chloride.

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Received February 16, 1957

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*Original Russian pagination. See C.B. Translation.

**In Russian.

SULFOLYSIS OF THE SULFONYL GROUPS IN AROMATIC SULFONIC ACIDS

F. M. Vainshtein and E. A. Shilov

A study of the migration of sulfonyl groups showed that these reactions proceed preferentially by the hydrolysis of sulfonic acids followed by the sulfonation of the aromatic compound formed [1]. However, cases are known where the sulfonyl groups were transferred in anhydrous sulfuric acid and even in oleum, i.e. under conditions which exclude hydrolysis [2,3]. Some authors considered this fact as proof of the intramolecular mechanism of the migration of sulfonyl groups in aromatic sulfonic acids [3]. But such a conclusion is difficult to accept on stereo-chemical grounds: for example, it is improbable that the sulfonyl groups of 1,5-naphthalenedisulfonic acid could actually move to positions 2 and 7 without their bond with the aromatic nucleus being broken for a moment. At the same time there would be no need to postulate the intramolecular mode of sulfonyl group migration in the absence of water, if we consider that the acceptor role of an SO_3 molecule may be taken over by other anionoids. In particular, sulfuric acid and its anion may combine with SO_3 to form pyrosulfuric acid and the anion $HS_2O_7^-$. Thus, the sulfonyl group migration could occur intermolecularly, not through hydrolysis but by passing through the stage of sulfolysis.

We decided to check this hypothesis, using sulfur S^{35} as a radioactive indicator. The investigations required sulfonic acids which were incapable of further sulfonation, as the introduction of radioactive sulfonyl groups into the unsubstituted positions in the molecule would have made the analysis of the exchange reactions more difficult. We chose, 2,4,6-toluenetrisulfonic acid (TTS) and 2,4,6-phenoltrisulfonic acid (PTS) for our experiments. The method consisted of heating each of these trisulfonic acids with radioactive fuming sulfuric acid or, on the contrary, the radioactive sulfonic acid was heated with nonradioactive oleum. Then the trisulfonic acid or H_2SO_4 was isolated from the reaction products, purified and its radioactivity determined.

EXPERIMENTAL

Preparations. 2,4,6-Toluenetrisulfonic acid was prepared by successive sulfonations of toluene by Claisen's method [4]. Toluenedisulfonic acid was obtained first and this was converted to its potassium salt and heated to 240° with HSO_3Cl. The excess sulfuric acid was removed with barium carbonate and the filtrate treated with potassium sulfate. After separation of the $BaSO_4$ precipitate, the filtrate contained the potassium salt of TTS with traces of the disulfonic acid. To prepare pure TTS, 1 mole of the potassium salt, dried at 130–140°, was mixed with 3 moles of PCl_5 and the mixture kept at 120–130° for 1 hour and then at 150° for half an hour. The excess PCl_5 was decomposed with cold water and the solid toluenetrisulfonyl chloride filtered onto a glass filter and treated with ether, which dissolved the toluenedisulfonyl chloride. The residue was recrystallized from chloroform until the melting point was 153°. The toluenetrisulfonyl chloride obtained was hydrolyzed by boiling under reflux with 14 parts of water. The filtered solution was evaporated on a water bath until the HCl had been removed completely. The yellow sirup obtained deposited white crystals of 2,4,6-toluenetrisulfonic acid after cooling. After being dried in vacuum over sodium hydroxide, the crystals contained 6 molecules of water per molecule of TTS according to analysis, which agreed with Claisen's data [4].

To prepare 2,4,6-phenoltrisulfonic acid, we heated phenol with chlorosulfonic acid for 5 hours at 130–140° [5]. The precipitate of phenoltrisulfonyl chloride formed was recrystallized twice from $CHCl_3$; the m.p. was 192°. The 2,4,6-phenoltrisulfonyl chloride was immediately hydrolyzed in water. After evaporation and cooling, the solution deposited crystals of PTS. The preparation was dried in vacuum and had the composition $C_6H_6O_{10}S_3 \cdot 3^1/_2\ H_2O$.

To prepare radioactive oleum or chlorosulfonic acid, we dissolved dry $Na_2S^{35}O_4$ in them.

The radioactivity was determined using such thin layers of the barium salts of the sulfonic acids that the self-absorption of the β-rays by the samples could be ignored. For these conditions, the thickness of the layers of TTS and PTS barium salts had to be not more than 6.5 mg/cm^2, and not more than 8 mg/cm^2 for $BaSO_4$. The precipitates were deposited on tared aluminum discs from fine suspensions in methanol. The weight was determined by difference after drying the sample at 100°. The emitting surface was 0.63 cm^2. The radioactivity was measured using an end-window tube housed in a lead castle and connected to a B type counting unit. Each radioactivity determination was repeated several times. We estimated the probable error in the average values at $\pm 3\%$.

We performed the experiments on the sulfolysis of sulfonic acids in sealed glass ampules, into which were placed from 0.07 to 0.1 g of TTS or PTS and sufficient radioactive or nonradioactive oleum (0.1–0.4 g) so that there remained excess SO_3 after the water of crystallization had been bound as H_2SO_4. The free SO_3 content was determined by analysis in control experiments. The ampules were heated for a known time in an aluminum block, the contents dissolved in water and the sulfuric acid precipitated with an aqueous suspension of $BaCO_3$. The filtrate was evaporated to dryness; samples were taken from the residue for activity determination. The percentage of exchange was calculated from the ratio of the observed radioactivity of the barium salt (R) to the calculated value for its activity at complete exchange (R_0).

Sulfolysis of 2,4,6-toluenetrisulfonic acid

A. Nonradioactive TTS was treated with radioactive oleum. The results of two experiments at 212° in this series are illustrated in Fig. 1. In the experiment illustrated by Curve 1, the free SO_3 content of the mixture was 8.5% and R_0 = 87 counts/mg/min. In the experiment illustrated by Curve 2, the free SO_3 content was 23% and R_0 = 300 counts/mg/min. Curves 1 and 2 show that in fuming sulfuric acid the sulfonyl groups of TTS undergo exchange at a measurable rate. The reaction was accelerated by increasing the SO_3 concentration in the fuming sulfuric acid.

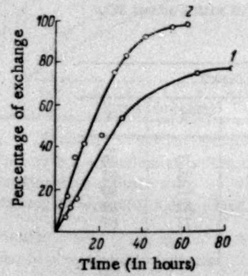


Fig. 1. Exchange of sulfonyl groups between 2,4,6-toluenetrisulfonic acid and radioactive fuming sulfuric acid. 1) 8.5% free SO_3, 2) 23% free SO_3.

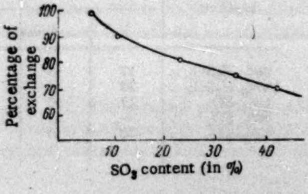
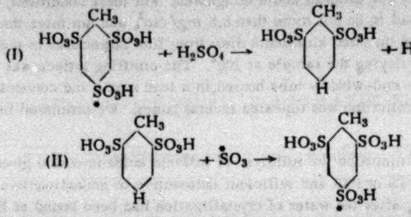


Fig. 2. Exchange of sulfonyl groups between radioactive 2,4,6-toluenetrisulfonic acid and nonradioactive fuming sulfuric acid with various SO_3 contents.

B. On the other hand, if the sulfolysis was performed in nonradioactive fuming sulfuric acid on radioactive TTS, then the percentage of exchange decreased with an increase in the SO_3 content of the mixture. The appropriate data are illustrated in Fig. 2 and are taken from a series of experiments performed at 212°. R_0 = 80–180 counts/mg/min and the heating time was 9 hours.

To explain this difference in the results from two identical exchange processes, one should take into consideration the fact that the reaction products examined in series A and B were not the same. In the first series we determined the radioactivity of the final product of sulfonation in the form of 2,4,6-toluenetrisulfonic acid and in the second, the radioactivity of the sulfuric acid, which controls the elimination and transfer of the sulfonyl group in the solution. At the same time, according to our postulate, the exchange of sulfonyl groups proceeds in two stages: I—actual sulfolysis of one or two sulfonyl groups, II—sulfonation.



Apparently, the reaction rate is limited by stage II and stage I proceeds relatively quickly. Therefore, if we consider series B, which is illustrated in the scheme, the radioactive sulfur will appear in the sulfuric acid at the rate of the sulfolysis. At the same time, when we determine the radioactivity of the TTS as in series A, we will observe the slower sulfonation of toluenedisulfonic acid. Therefore, increasing the SO_3 content retards stage I as it reduces the concentration of the proton donor—the H_2SO_4 molecule. On the other hand, the rate of stage II is increased by increasing the SO_3 content as together with this we are increasing the concentration of SO_3H^+, which is apparently the most active sulfonating agent [6].

2,4,6-Phenoltrisulfonic acid

The exchange was carried out at 115° with various concentrations of SO_3 in the mixture. The results of experiments with nonradioactive PTS and radioactive oleum are given in the Table and in Fig. 3.

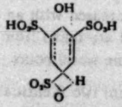
TABLE

Exchange of Sulfonyl Groups (in Percent) Between Nonradioactive 2,4,6-phenoltrisulfonic Acid and Radioactive Sulfuric Acid with Various SO_3 Concentrations.

Medium	Heating time (in hours)					
	1	2	3	4	5	7
94% H_2SO_4	17	53	60	70	79	80
100% H_2SO_4	22	54	59	66	75	83
11% SO_3	17	50	60	68	—	89
34% SO_3	—	53	61	75	82	86
47% SO_3	16	53	—	69	77	87

The figures given in the Table show that the rate of exchange in PTS does not depend on the concentration of SO_3 in the mixture. This remarkable relationship apparently has to be explained by the fact that rate of SO_3H exchange firstly limits the total reaction rate and secondly, this reaction does not require H_2SO_4 as the SO_3H acceptor.

It is possible that the proton donor is a sulfonyl group of the phenoltrisulfonic acid itself and the exchange proceeds through an intermediate complex.



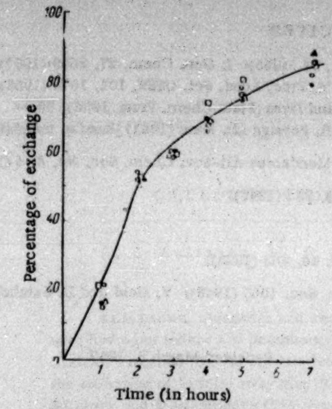


Fig. 3. Exchange of sulfonyl groups between nonradioactive 2,4,6-phenoltrisulfonic acid and radioactive sulfuric acid with various SO_3 concentrations.

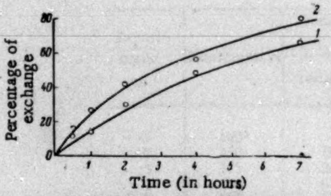


Fig. 4. Exchange of sulfonyl groups between radioactive 2,4,6-toluenetrisulfonic acid and nonradioactive sulfuric acid. 1) Without additions, 2) with 20% K_2SO_4 added.

Fuming sulfuric acid is only an inert solvent in the first stage and the stage of PTS sulfonation proceeds relatively rapidly and does not affect the total exchange rate.

Exchange experiments with 2,4,6-toluenetrisulfonic acid in aqueous sulfuric acid

Several experiments with TTS were performed under conditions where hydrolysis of sulfonyl groups was possible, namely, in 91% sulfuric acid. In this case we used radioactive TTS and nonradioactive sulfuric acid and therefore observed the rate of stage I (Fig. 4). Because of the increase in reaction rate, the reaction temperature could be lowered to 175°. Nevertheless, heating was accompanied by tar formation and oxidation, which appeared as darkening and the evolution of SO_2. At the same time, these effects were hardly noticeable during heating in oleum.

Some experiments were carried out with K_2SO_4 added as an acceptor for HO_3S groups. As Fig. 4 shows, large additions of sulfate (20%) accelerate the reaction noticeably, confirming the acceptor action of K_2SO_4. The addition of 3% of this material did not produce a noticeable effect. This is readily understood as potassium sulfate competes with water as a proton acceptor.

We should also like to mention the fact that using the information on the catalytic effect of anhydrous ferric chloride on the rearrangement of 1,5-naphthalenedisulfonic acid [2], we performed experiments on the exchange of sulfonyl groups by radioactive PTS in the presence of $FeCl_3$, but the addition of this material had no effect.

SUMMARY

1. The exchange of sulfonyl groups of 2,4,6-toluenetrisulfonic acid (TTS) at 212° and 2,4,6-phenoltrisulfonic acid (PTS) at 115° with fuming sulfuric acid, containing various amounts of SO_3, was studied. S^{35} was used as a radioactive indicator.

2. It was shown that the exchange of sulfonyl groups in TTS proceeded in two stages: I - the substitution of the HO_3S group by H (sulfolysis) and II - the sulfonation of the sulfolysis product to TTS. Stage I was retarded and stage II accelerated by an increase in the SO_3 content of the sulfuric acid.

3. The rate of the HO_3S group exchange in PTS did not depend on the SO_3 concentration in the sulfuric acid.

4. It was postulated that the mechanism of TTS sulfolysis involved the participation of SO_3 acceptors in the form of sulfuric acid, which is converted to pyrosulfuric acid. It is possible that in PTS sulfolysis a sulfonyl group of the PTS molecule itself was the proton donor.

5. The exchange of sulfonyl groups of TTS with 91% aqueous sulfuric acid was accelerated by adding K_2SO_4.

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Received March 5, 1957

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* Original Russian pagination. See C.B. Translation.

** In Russian.

*** As in original — Publisher's note.

CATALYTIC REDUCTION OF BENZALDEHYDE

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As is known, aldehydes and ketones may be converted into hydrocarbons by reduction with hydrogen iodide and phosphorus [1,2, 4–8] or through appropriate hydrazones by Kizhner's method [3]. In the last few years, a number of papers have been published on the reduction of furfural to sylvan [9–15] and benzaldehyde to toluene [16–22]. Recently Sultanov and Maslennikova [23] proposed a new copper-zinc-aluminum alloy catalyst, similar to Devarda's alloy, for the reduction of furfural to sylvan.

In this work we studied the reduction of benzaldehyde over this copper-zinc-aluminum catalyst. The results are given in Table 1.

TABLE 1

Experiment no.	Temperature	Content of products in catalyzate (in %)			Losses (in %)
		toluene	benzyl alcohol	benzaldehyde	
1	100°	—	—	100	—
2	150	19.0	53	16.6	11.4
3	175	26.2	54	6.6	13.2
4	200	63.5	11.4	6.6	18.5
5	225	87.0	1.6	—	11.4
6	300	87.4	2.4	–	10.2

The data in Table 1 show that the best results in the reduction of benzaldehyde to toluene over the copper-zinc-aluminum catalyst were obtained in the temperature range of 200–300°. The considerable losses apparently were mainly because of the process being intermittent, for when it was carried out continuously at 250° the losses were reduced to 5% with a toluene yield of 91% and a 4% yield of benzyl alcohol.

The reaction mechanism of benzaldehyde reduction to toluene using various catalysts has hardly been studied. According to the data given by Ipatiev, benzaldehyde is reduced on an iron surface through the intermediate stage of benzyl alcohol formation [18]. Such a mechanism is also possible on precipitated copper catalysts, supported on dehydrogenating substances such as clay, oxides of aluminum, chromium and thorium, silicon dioxide etc. As carbonyl compounds are reduced on these catalysts at relatively high temperatures, the hydroxyl groups of the intermediate alcohols may be substituted by hydrogen atoms. As benzaldehyde was reduced on our catalyst at quite a low temperature (from 150 to 300°) and the catalyst contained metallic zinc, this reaction on the copper-zinc-aluminum catalyst may be compared with Clemmensen's reaction.

It is interesting to note that the reduction of benzaldehyde to toluene by Clemmensen's method gave a considerable yield of the latter. However, under the same conditions benzyl alcohol gave not more than 6% of toluene, as our tests showed. Also a small amount of benzyl chloride and a great deal of an undistillable liquid with a sharp smell, were isolated from the residue. These data contradict the carbinol mechanism of benzaldehyde reduction by Clemmensen's reaction and raise doubts on the carbinol mechanism of benzaldehyde reduction to toluene on a copper-zinc-aluminum catalyst as well. Characteristically, furfural gave up to 85% of sylvan on a copper-zinc-aluminum catalyst at 225-250° while under the same conditions furfuryl alcohol gave only a 45% yield of sylvan.

These data seem to indicate that the reduction of the aldehyde group to the methyl group does not proceed through a stage of alcohol formation, but directly. In order to confirm this hypothesis we passed benzyl alcohol through the catalyst without introducing hydrogen from outside. This gave benzaldehyde (see Table 2) in decreasing yield with increased temperature, and toluene in increasing yield with increased temperature. On this basis, one may consider that the reaction begins with dehydrogenation of the benzyl alcohol. The fall in benzaldehyde yield with increasing temperature and the rise in toluene yield are apparently a result of the more intense reduction of benzaldehyde to toluene than to alcohol and not inhibition of the reaction by dehydrogenation of the alcohol.

TABLE 2

Experiment no.	Temperature	Content of products in catalyzate (in %)			Losses (in %)
		benzaldehyde	toluene	benzyl alcohol	
1	150°	68.0	16.9	11	4.1
2	200	59.6	27.4	10	3.0
3	250	57.9	32.4	6.6	3.1
4	300	39.0	58.5	0.0	2.5

On the other hand, the data obtained show that the temperatures 250–300°, at which benzaldehyde is successfully reduced, are most unsuitable for the existence and therefore, the formation of benzyl alcohol from benzaldehyde. In the fourth experiment in Table 2, the toluene yield does not correspond to the consumption of hydrogen evolved during dehydrogenation of the benzyl alcohol. This may be explained by the participation of hydrogen, chemosorbed on the catalyst surface.

A smaller amount of furfuryl alcohol was converted to furfural and sylvan at 225–250° than benzyl alcohol to benzaldehyde and toluene: only 19.3% of furfural and 12% of sylvan were formed.

Benzyl alcohol was successfully converted to toluene on the copper-zinc-aluminum catalyst when it was passed through with hydrogen (Table 3) which was apparently due to the ease with which this alcohol is dehydrogenated.

TABLE 3

Experiment no.	Temperature	Content of products in catalyzate (in %)			Losses (in %)
		toluene	benzyl alcohol	benzaldehyde	
1	150°	52.5	46	0	1.5
2	200	75.6	23	0	1.4
3	250	90	5.9	0	4.1

The absence of traces of benzaldehyde during benzyl alcohol reduction (Table 3) may also be explained by the fast conversion of benzaldehyde to toluene. Therefore, the benzyl alcohol residue in experiments 2 and 3 (Table 3) are greater than the alcohol yields in experiments 4–6 (Table 1), in spite of the large excess of hydrogen used in the experiments in Table 3. Finally, it is interesting to note that ethyl alcohol was not dehydrogenated to acetaldehyde in the range 200–350° on the copper-zinc-aluminum catalyst and that no noticeable reduction to ethane occurred in a current of hydrogen; in connection with the acetaldehyde, at 200–350° it was completely hydrogenated in a current of hydrogen to ethyl alcohol. No ethane formation was observed in this experiment.

These data indicate that benzaldehyde reduction to toluene on a copper-zinc-aluminum catalyst proceeds directly, while benzyl alcohol is converted to toluene mainly through benzaldehyde. The same may be said of furfural and furfuryl alcohol under the same conditions.

EXPERIMENTAL

A reactor consisting of a stainless steel tube, 40 mm in diameter and 650 mm high, was placed in a vertical furnace with a temperature control device. A 400 mm layer of catalyst was placed exactly in the center of the reactor. This required 500 ml of granulated catalyst weighing 800 g and with a particle diameter of 3–4 mm. A thermocouple housing was passed through the lid into the center of the reactor. Materials were fed into the reactor from a burette at the top, under slight pressure. The catalyzate (together with excess hydrogen) was led through a normal cooling system, cooled with ice then with solid carbon dioxide. The starting material was fed in at a rate of 60 ml/hour with a 5 molar amount of hydrogen.

The preparation method, quantitative composition and activation method for the catalyst were described previously [23].

Reduction of benzaldehyde (Table 1, experiment 4). 60 ml of benzaldehyde (62.76 g) was steadily fed into the reactor from the burette over a period of 1 hour with the catalyst bed at 200°. At the same time, hydrogen was fed in at a rate of 66.5 liters/hour, while the excess escaped into the atmosphere. The catalyzate passed from the reactor, through a water condenser and into a receiver, cooled with an ice mixture. For the condensation of possible volatile products, another receiver was attached and this was cooled with solid carbon dioxide. After removal of the aqueous layer, the whole catalyzate was treated with sodium bisulfite solution to remove benzaldehyde. Toluene and benzyl alcohol were separated by a normal distillation. We obtained 4.2 g (6.6%) of benzaldehyde, 34.6 g (63.5%) of toluene with b.p. 108–110°, $n^{20}D$ 1.4952 and 7.3 g (11.4%) of benzyl alcohol with b.p. 200°, $n^{20}D$ 1.5396 (benzyl bromide was prepared).

Reduction of furfural. 100 ml of furfural was fed into the reactor steadily over a period of 3 hours 20 minutes at 225–250°. During this period 230 liters of hydrogen was passed in. The aqueous layer was separated from the combined catalysts from the two receivers and the catalyzate dried over anhydrous sodium sulfate. Distillation of the dried catalyzate from a normal flask with a pear fractionating column gave 92 ml of sylvan (85% of the furfural used) with b.p. 60–65°, $n^{20}D$ 1.4340 and 6 ml (12%) of furfuryl alcohol with b.p. 165–172°, $n^{20}D$ 1.4860.

Reduction of furfuryl alcohol. 30 ml (33.9 g) of pure furfuryl alcohol was passed through the reactor over a period of 60 minutes at 225–250° simultaneously with 60 liters of hydrogen. The aqueous layer was separated from the total catalyzate (31 ml), which was then dried over anhydrous sodium sulfate. We isolated 14.5 ml or 13.3 g of sylvan (45% of the starting alcohol) and 15 ml of a high-boiling fraction, from which 1.5 ml (1.7 g) of furfural was isolated by the bisulfite method. The residue contained 14.6 ml (16.5 g) of furfural alcohol (48.7%) with b.p. 166–172°, $n^{20}D$ 1.4860.

Conversion of furfuryl alcohol on the catalyst. 24 ml (27 g) of furfuryl alcohol was fed in over a period of 60 minutes at 225–250° without a stream of hydrogen. We isolated 4.4 ml (5 g) of furfural (19.2%) from the dried catalyst by the bisulfite method and the residue yielded 3 ml (12.1%) of sylvan and 14 ml (15.7 g) of furfuryl alcohol (58%).

Conversion of benzyl alcohol on the catalyst (Table 2, experiment 3). 60 ml (62.6 g) of benzyl alcohol was passed through the catalyst bed at 250° over a period of 1 hour without hydrogen. The dried catalyst yielded 17.3 g of toluene (32.4%), 35.5 g of benzaldehyde (57.9%) and 41.7 g of benzyl alcohol (6.6%).

Reduction of benzyl alcohol (Table 3, experiment 2). 60 ml (62.6 g) of benzyl alcohol and 66.5 liters of hydrogen were passed through the catalyst bed at 200° over a period of 1 hour. From the catalyzate we isolated 39 g of toluene (75.6%) and 14.6 g of benzyl alcohol (23%).

Conversion of ethyl alcohol on the catalyst in a stream of hydrogen. 30 ml of ethyl alcohol and 60 liters of hydrogen were passed through the catalyst at 250 and 300° over a period of 1 hour. The catalyzate was unchanged alcohol. Analysis of the gases for hydrocarbons gave a negative result.

Conversion of ethyl alcohol on the catalyst without the addition of hydrogen. With the catalyst at 250 and at 300°, 30 ml of ethyl alcohol yielded 27 ml of liquid, which was identified as ethyl alcohol. A qualitative reaction for aldehyde was negative.

Conversion of actaldehyde on the catalyst in a stream of hydrogen. 30 ml of acetaldehyde and 60 liters of hydrogen were fed in over a period of 1 hour at 225°. We obtained 24.1 ml of catalyzate, which was dried; this yielded 23.8 g (93.5%) of ethyl alcohol, boiling at 78–80°, with $n^{20}D$ 1.3618. Analysis for hydrocarbons was negative.

Reduction of benzyl alcohol under the conditions of the Clemmensen reaction. 200 g of amalgamated zinc and 150 ml of hydrochloric acid were placed in a liter flask, fitted with a reflux condenser. When the vigorous evolution of hydrogen began, benzyl alcohol (50 g) was introduced dropwise into the sphere of the reaction over a period of 1 hour, then the mixture was boiled for 2 hours with the portionwise addition of a further 50 ml of concentrated hydrochloric acid during this time; the contents of the flask were then diluted with 200 ml of water and the upper, oily layer separated, dried over sodium sulfate and distilled. We isolated 3 ml (6%) of toluene with b.p. 110° and 12 ml of benzyl chloride (24%) with b.p. 178–179°. The residue was an undistillable liquid with a sharp smell and we did not examine it further.

SUMMARY

1. The possibility of using a copper-zinc-aluminum alloy catalyst for reducing benzaldehyde and benzyl alcohol to toluene in a flow system under ordinary pressure was demonstrated.

2. In the absence of hydrogen, benzyl and furfuryl alcohols were dehydrogenated to the corresponding aldehydes, forming simultaneously toluene and sylvan with the hydrogen evolved during the reaction.

3. Benzaldehyde was reduced on a copper-zinc-aluminum catalyst directly without the intermediate formation of benzyl alcohol. The alcohol then formed was the product of a parallel hydrogenation process which occurred mainly at temperatures below the optimal temperatures for the reduction. Under these conditions the alcohols, capable of being dehydrogenated to aldehydes, may be converted to hydrocarbons.

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Received October 23, 1957

INVESTIGATION OF OXIDO COMPOUNDS

X. REACTION OF α-OXIDES OF ALLYL ETHERS OF PHENOL, o- AND p-CRESOLS AND GUAIACOL WITH AMINES

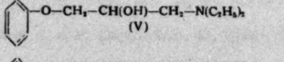
Z. B. Idel'chik and V. I. Pansevich-Koliada

As is known, some derivatives of α-oxides of phenyl allyl ethers are physiologically active preparations [1,2]. Some derivatives of α-oxides of nitrophenyl allyl ethers also possess this property [3].

In order to increase the information available on such compounds, in the present work we reacted α-oxides of the allyl ethers of phenol, o- and p-cresols and guaiacol with diethylamine and α-oxides of the allyl ethers of phenol and o-cresol with piperidine.

Oxidation of the allyl ethers of appropriate phenols with acetyl hydroperoxide [4,5] and reaction of the phenols with epichlorohydrin [1,2,6–9] gave the following α-oxides of phenyl allyl ethers: 1-phenoxy-2,3-oxidopropane (I), 1-(o-tolyloxy)-2,3-oxidopropane (II), 1-(p-tolyloxy)-2,3-oxidopropane (III) and 1-(o-methoxyphenoxy)-2,3-oxidopropane (IV).

Gentle heating of the ether oxides obtained (I, II, III, IV) with diethylamine [1,2,6,7,10], and the ether oxides (I and II) with piperidine gave the corresponding phenoxyamino alcohols. On the basis of certain papers [1,2] on the reaction of glycide ethers of phenol with amines, the structures of the phenoxyamino alcohols we obtained may be expressed by the following formulas. (V–X): 1-phenoxy-3-diethylamino-propanol-2 (V), 1-(o-tolyloxy)-3-diethylaminopropanol-2 (VI), 1-(p-tolyloxy)-3-diethylaminopropanol-2 (VII), 1-(o-methoxyphenoxy)-3-diethylaminopropanol-2 (VIII), 1-phenoxy-3-(N-piperidyl)-propanol-2 (IX) and 1-(o-tolyloxy)-3-(N-piperidyl)-propanol-2 (X).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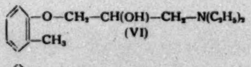
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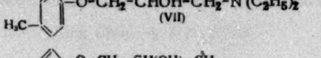
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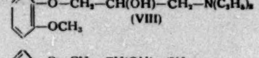
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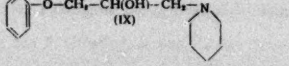
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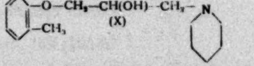
(X)

All the phenoxyamino alcohols mentioned above readily formed water-soluble hydrochlorides and ethiodides. Substances (VI, IX and X) were obtained only in the form of derivatives.

Pharmacological testing of the phenoxyamino alcohols (V–X) and their hydrochlorides and ethiodides showed that they have a strong hypotensive effect with relatively low toxicity.* The toxicity increased from free phenoxyamino alcohols to their hydrochlorides and ethiodides, but the hypotensive effect of these preparations increased in the same sequence.

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* The tests were carried out by L. A. Iakubovich in the pharmacology department of the Minsk Medical Institute.

EXPERIMENTAL

1. 1-Phenoxy-3-diethylaminopropanol-2 (V). The α-oxide of the allyl ether of phenol (I) was prepared by oxidizing allyl phenyl ether with acetyl hydroperoxide [4,5] and also by reacting phenol with epichlorohydrin [1,2,6–8] and appeared as a mobile liquid with a weak, tobacco-like smell.

B.p. 242.5° (755 mm), 104° (2 mm), n^{20}_D 1.5300, d^{20}_4 1.1190, MR_D 41.54; calculated 41.37.

26 g of diethylamine was added to 23 g of (I) and the mixture heated on a water bath at 60–65° for 5 hours. The excess diethylamine was washed out with water and the reaction products extracted with ether, dried with $MgSO_4$ and vacuum distilled. The substance obtained was a thick liquid, which rapidly darkened in air and was insoluble in water and readily soluble in organic solvents.

B.p. 176–178° (17 mm), n^{20}_D 1.5090, d^{20}_4 1.0200, MR_D 65.57; calculated 65.74.

Found %: C 70.01; H 9.79. M 226.1. $C_{13}H_{21}O_2N$. Calculated %: C 70.00; H 9.41. M 233.

Ethiodide. 15 g of (V) and 10.5 g of ethyl iodide were heated under reflux on a water bath for 3 hours. The excess ethyl iodide was distilled off by gentle heating in vacuum and then several recrystallizations from an alcohol–ether mixture yielded yellowish crystals, readily soluble in cold water. The m.p. was 119°.

Hydrochloride. 19 g of (V) was dissolved in 50 ml of absolute ether and dry hydrogen chloride passed into the solution until no more crystals were deposited. The hydrochloride was a liquid at room temperature. On cooling with snow, it formed pretty scales, which were readily soluble in cold water and alcohol.

2. 1-(o-Tolyloxy)-3-diethylaminopropanol-2 (VI). The α-oxide of the allyl ether of o-cresol (II) was prepared by reacting o-cresol with chlorohydrin.

B.p. 123–125° (2 mm), n^{20}_D 1.5290, d^{20}_4 1.0884, MR_D 46.47; calculated 45.99.

We should note that oxidation of the allyl ether of o-cresol with acetyl hydroperoxide gave an extremely low yield of the α-oxide of this ether [4].

30 g of (II) and 20 g of diethylamine were heated at 65–70° on a water bath for 4 hours. The diethylamine was washed out with water and the reaction product dried and used for the preparation of the ethiodide and the hydrochloride without distillation.

Ethiodide. 20 g of (VI) and 20 g of ethyl iodide were heated on a water bath at 30–35° for half an hour. The whole material crystallized overnight. Recrystallization from an alcohol ether mixture yielded 7.0 g of a substance which was readily soluble in water. The m.p. was 141.5°.

Hydrochloride. 20 g of (VI) was dissolved in 50 ml of absolute ether and dry hydrogen chloride passed in until no more crystals were deposited. We obtained 16.5 g of the hydrochloride, which was readily soluble in cold water and alcohol. The m.p. was 107° (from an alcohol–ether mixture).

3. 1-(p-Tolyloxy)-3-diethylaminopropanol-2 (VII). 5 g of (III), prepared by oxidizing the allyl ether of p-cresol with acetyl hydroperoxide [5] and by reacting p-cresol with epichlorohydrin [1,2,6–8], was treated with 5.5 g of diethylamine (1 : 2.5 moles). After being heated on a water bath at 60–70° for 4 hours, the reaction mixture had a blood red color. The diethylamine was removed under reduced pressure and the residue vacuum distilled. We obtained 5.8 g of substance.

B.p. 139.5° (1.5 mm), n^{20}_D 1.5070, d^{20}_4 1.0055, MR_D 70.15; calculated 70.32.

Found %: C 70.48; H 10.00; N 5.66. M 241.3, 233.9. $C_{14}H_{23}O_2N$. Calculated %: C 70.88; H 9.70; N 5.90. M 237.

Ethiodide. 5 g of (VII) was heated with 3.6 g of ethyl iodide on a water bath at 50° for one and a half hours. On cooling the ethiodide crystallized. Two reprecipitations from alcohol with ether yielded 3 g of substance with m.p. 135.5°.

The hydrochloride of 1-(p-tolyloxy)-3-diethylaminopropanol-2 (VII) was obtained as a thick oil. It was readily soluble in cold water and alcohol.

4. 1-(o-Methoxyphenoxy)-3-diethylaminopropanol-2 (VIII). The α-oxide of the allyl ether of guaiacol was prepared by oxidizing the allyl ether of guaiacol with acetyl hydroperoxide [5].

4 g of the oxide was heated with 4 g of diethylamine (1 : 2.5 moles) on a water bath for 3 hours. After evaporation of the diethylamine, the reaction product was vacuum distilled. We obtained 4 g of substance as a thick, slightly pinkish liquid.

B.p. 167° (5.5 mm), n_D^{20} 1.5153, d_4^{20} 1.0631, MR_D 71.51; calculated 71.98.

Found %: C 66.54; H 9.23. M 248.2. $C_{14}H_{23}O_3N$. Calculated %: C 66.40; H 9.09. M 253.

Ethiodide. 2.5 g of (VIII) and 1.54 g of ethyl iodide were heated on a water bath at 60° for 5 hours. After several days, the whole mixture had crystallized. Two recrystallizations from an alcohol – ether mixture yielded 2 g of the ethiodide with m.p. 104°.

5. Hydrochloride of 1-phenoxy-3-(N-piperidyl)-proponal-2 (IX). To 2 g of the oxide of allyl phenyl ether (I), dissolved in 3 g of alcohol, was added 1.3 g of piperidine. The mixture was heated on a water bath for 2.5 hours. The alcohol and the piperidine were distilled off in vacuum. The residue crystallized. After recrystallization from an alcohol – ether mixture, the substance (IX) was again dissolved in a mixture of alcohol and ether and dry hydrogen chloride passed through this solution until no more crystals were deposited. The hydrochloride was recrystallized from a mixture of alcohol and ether. We obtained 3.0 g of a substance with m.p. 126.5°.

6. Hydrochloride of 1-(o-tolyloxy)-3-(N-piperidyl)-propanol-2 (X). To 3 g of the α-oxide of allyl o-cresyl ether (II), dissolved in 3 g of ethyl alcohol, was added 1.5 g of piperidine. The mixture was heated on a water bath for 3 hours. The alcohol and piperidine were distilled off in vacuum. The residue crystallized. It was dissolved in ether and dry hydrogen chloride passed through the cooled solution. The hydrochloride obtained was dissolved in alcohol and precipitated with ether. We obtained 4.5 g of white crystals. The m.p. was 119°.

SUMMARY

Reaction of α-oxides of allyl ethers of o- and p-cresols and guaiacol with diethylamine and α-oxides of allyl ethers of phenol and o-cresol with piperidine gave the following phenoxyamino alcohols: 1-phenoxy-3-diethylaminopropanol-2, 1-(o-tolyloxy)-3-diethylaminopropanol-2, 1-(p-tolyloxy)-3-diethylaminopropanol-2, 1-(o-methoxyphenoxy)-3-diethylaminopropanol-2, 1-phenoxy-3-(N-piperidyl)-propanol-2 and 1-(o-tolyloxy)-3-(N-piperidyl)-propanol-2. Their ethiodides and hydrochlorides were prepared.

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Received March 28, 1957

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* Original Russian pagination. See C.B. Translation.

THE NUMBER OF STABLE OXIDES FORMED BY THE METALS OF THE LONG PERIODS OF THE PERIODIC SYSTEM

S.A. Shchukarev

In 1945 I published an article [1] on the thermal stability of the oxides of manganese and iron, which contained the foundations of a number of thermodynamic postulates essential for the development of the study of those series of chemical compounds of stable form which result from the combination of two individual elements, for example, a given metal and oxygen.

The present work represents a further development and generalization of these postulates.

From as far back as the time of D.I. Mendeleev, eight typical oxide forms have been recognized, corresponding to different degrees of oxidation of the element for whose compounds these forms are established. Particular importance is attached in this connection to the limiting forms of the saturated compounds, and also to the question of which elements are capable of showing more than one form of chemical behavior. In this latter respect, as is well known, considerable differences are observed between elements. Thus, for example, sodium has only one form NaX, while manganese has a whole series of competing forms, a list of which resembles in appearance the series of stable isotopes of an element

$$- MnX_2\ MnX_3\ MnX_4 - MnX_6\ MnX_7$$

The form MnX is not found, as a result of its instability, and MnX_2 represents the lower limit of the series of compounds whose existence has been experimentally established; the upper limit of the series, corresponding to the group number of seven, is the form MnX_7, the compound MnX_8 being unstable and absent. In addition there is a gap in the series between MnX_2 and MnX_7 corresponding to the disappearance of the unstable form MnX_5. We may regard the upper limiting form MnX_7, corresponding to the number of outer electrons, to be saturated with manganese.

Turning our attention to an examination of some concrete examples of oxide series, we shall select first of all elements forming oxides which are gaseous under ordinary conditions and thus first of all eliminate the complicating influence of such important factors as the energy of condensation and the crystal lattice geometry.

Let us consider the oxides of carbon, nitrogen and oxygen, with analogous formulas:

$$\begin{gathered} C,\ CO,\ CO_2 \\ N,\ NO,\ NO_2,\ NO_3 \\ O,\ OO,\ OO_2 \end{gathered}$$

All of these substances have a central atom to which oxygen atoms are attached. The three series of oxides consist of successive states obtained by the addition of first one and then a second oxygen atom; the addition of a third oxygen atom, resulting in a neutral molecule, is observed only in the formation of the extremely unstable, uncharged free radical NO_3.

Table 1 below gives the energies of formation of the above-mentioned oxides from the free atoms.

The data from Table 1 have been used to construct Figure 1, from which it can be seen that the addition of each successive oxygen atom produces a smaller effect than the addition of the preceding atom; the curves fall less and less steeply, as if anticipating the approach of the saturation state, after which the curve should

TABLE 1

Oxide	Energy of formation (in kcal.)	Δ	Oxide	Energy of formation (in kcal.)	Δ	Oxide	Energy of formation (in kcal.)
CO . . .	− 256	126	CO_2 . .	− 382	-	—	−
NO . . .	− 149	72	NO_2 . .	− 221	51	NO_3 . . .	− 272
OO . . .	− 118	24	OO_2 . .	− 142	-	—	—

start to move upwards. The three curves lie in a definite sequence one below the other: the greatest attractive force is evidently that between the oxygen atoms and carbon.

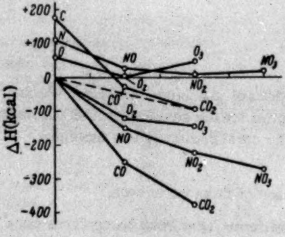

Fig. 1. The energies of formation of oxide molecules for oxygen, nitrogen and carbon from the free atoms (lower group of curves) and from the simple substances (upper group of curves).

If the oxides are prepared not from the free atoms but from the simple substances, energy has first of all to be used up in atomizing the latter. When this factor is taken into consideration, we obtain the values given in Table 2 for the energies of formation of the gaseous molecules from the simple substances.

Since the work of atomization in some cases exceeds the energy of interaction of an oxygen atom with the atoms of the oxidized substance, some of the effects obtained are endothermic.

When the data from Table 2 are added to Figure 1, we obtain three new curves which lie above the previous set.

The starting points of the original curves are raised by 170, 111 and 59 kcal. respectively; the points corresponding to the compounds with formulas RO, RO_2 and RO_3 are raised to different extents:

	RO	RO_2	RO_3
In the case of carbon	170 + 59	170 + 2·59	—
In the case of nitrogen	111 + 59	111 + 2·59	111 + 3·59
In the case of oxygen.	59 + 59	59 + 2·59	—

Thus the farther a point on Figure 1 lies to the right, the higher it is raised in comparison with the points on the same curve which lie to its left. This factor changes the shape of the curves, and, in particular, results in the appearance of minima (for NO_2 and O_2); this is explained by the fact that the vertical distance between the NO_2 and NO_3 points is equal to 51 kcal. on the original curve, i.e., it is less than 59 kcal.; in exactly the same way distance between the O_2 and O_3 points is equal to 24 kcal., i.e., less than 59 kcal. From this it is clear that NO_3 and O_3 are capable of liberating part of their oxygen exothermically. It is in this way that the upper limit of stable oxide formation for a particular element may be lowered.

TABLE 2

Atom	Energy of atomization per g-atom (kcal.)	Oxide	Energy of formation (kcal.)	Oxide	Energy of formation (kcal.)	Oxide	Energy of formation (kcal.)
[C]	+ 170	(CO) . . .	− 27	CO_2. . .	− 94	−	−
(N)	+ 111	(NO) . . .	+ 21	NO_2. . .	+ 8	NO_3. . . .	+ 16
O	+ 59	OO	0	OO_2. . .	+ 35	−	−

The fairly high energy of atomization of molecular nitrogen and the higher position of the original curve for its oxides compared with the oxides of carbon makes the formation of all the oxides of nitrogen endothermic. In spite of the fact that the energy of atomization of graphite is even higher, the starting position of the CO and CO_2 points is so low that even after they have been raised to the new curves they still lie in the exothermic region; the CO point, however, lies above the broken line connecting the CO_2 point to the origin. Consequently, CO is capable of exothermic decomposition to carbon and CO_2.

$$\underset{+54}{CO} - 40 = [C] + \underset{-94}{CO_2}$$

Thus the lower limit of thermodynamic stability for the oxides of carbon is shifted at low temperatures from CO to CO_2. It is evident that, as in the case of CO, the lower states of oxidation in many other cases may become unstable for elements which have high sublimation energies in the form of the simple substances.

Many other phenomena are dependent on the competition between simple substances and compounds consisting of atoms of different type . Thus, for example, in the formation, from the free atoms, of the oxides and hydrogen compounds of carbon, the quantities of energy liberated are of similar magnitude; in the formation of CH_4 slightly more energy is evolved, even, than in the formation of CO_2 (396 kcal. > 382 kcal.) One has only to consider the formation of the compounds from the simple substances, however, and the picture is altered; CH_4, in fact, becomes a much less stable substance than CO_2. This results from the fact that the atomization of two moles of H_2 requires 208 kcal., while the atomization of one mole of O_2 requires only 118 kcal., i.e., in the first case 90 kcal. more are required. Such molecules as CH, CH_2, CH_3 are all found in the endothermic region and appear as free radicals. These relationships are clearly shown in Figure 2 and in Table 3 [2].

TABLE 3

	Energy of formation (in kcal.)			Energy of formation (in kcal.)	
	from the atoms	from simple substances		from the atoms	from simple substances
C	0	+170			
CH	— 89	+133	$\frac{1}{2}C_2$	— 75	+95
CH_2	—190	+ 84			
CH_3	—286	+ 40	$\frac{1}{2}C_2H_2$ . . .	—195	+27
CH_4	—396	— 18			
CH_5	—388	+42	$\frac{1}{2}C_2H_4$ . . .	—270.5	+ 3.5
			$\frac{1}{2}C_2H_6$ . . .	—337.5	—11.5

From an examination of Figure 2 we can see that the exothermic phenomena of polymerization of the unsaturated molecules C, CH, CH_2 and CH_3 lead to the formation of dimers, one of which – ethane – now lies in the exothermic region. In addition it should be noted that the question of whether the molecule is odd or even in the sequence evidently has some influence on the energies of formation of the monomeric molecules. Thus, the energies of the successive additions of the second and fourth H atoms, which make the molecules even, are accompanied by a great evolution of energy; as a result, the points lie not on a single curve but on two curves (like the energies of the odd and even isotopes in the series for a given element). It is true that the distance between the curves is small, and after dimerization the phenomenon becomes obscured, since the energies of dimerization decrease regularly from C_2H_2 to C_2H_6.

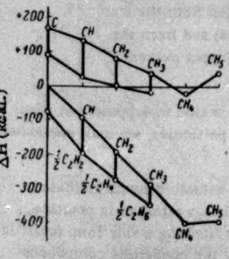

Fig. 2. The energy of formation of hydrocarbons from the free atoms (lower curves) and from the simple substances (upper lines).

In the case of the oxides of hydrogen, as can be seen from Figure 3, the division into odd and even curves is much more clearly defined. At the same time the curves have changed places (as in the case of the isotope series,) the even curve lying not below but above the odd curve, which is related to the fact that hydrogen is the opposite of the even element carbon, i.e., of the artiad element, the hydrogen itself being an odd element (perissad). Figure 3 was constructed using the data [2] given in Table 4.

TABLE 4

	Energy of formation (kcal.)	
	from the atoms	from the simple substances
HO	− 104	+ 7
HO_2.	− 169	+ 1
½ H_2O.	− 111	− 30
½ H_2O_2	− 128	− 17

From the examples quoted, we see that gaseous molecules containing an odd number of atoms with even atomic number (i.e., perissad atoms) are less stable and are formed with a smaller evolution of energy. Such molecules strive by some means or other to alter their composition and, in particular, tend to dimerize; this yields molecules containing an even number of electrons.

The effect of the odd or even character of the atoms is even more clearly shown in the case of the oxides of nitrogen and chlorine (Table 5.)

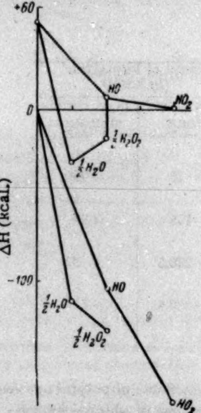

Fig. 3. The energies of formation of the oxides of hydrogen from the free atoms (lower curves) and from the simple substances (upper curves).

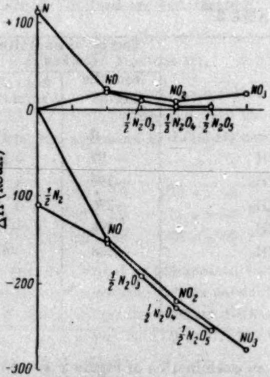

Fig. 4. The energies of formation of the oxides of nitrogen from the free atoms (lower curves) and from the simple substances (upper curves).

All that has been said above relates to gaseous compounds, and there is every reason to suppose that when we change to crystalline substances, and to refractory and nonvolatile substances in particular, we shall encounter a number of peculiar features, as D.I. Mendeleev repeatedly pointed out.

The fundamental state of affairs, in which it is found that the varieties of the saturated forms indicated by the periodic law and depending on the electronic structure of the atom are not always attained in practice, is also found for solid oxides and halides. The classical example of the fact that the limiting stable form found in practice does not always correspond to the theoretical saturation state is provided by the condensed compounds of vanadium; the compositions of the highest compounds given by this element with oxygen and fluorine are V_2O_5 and VF_5, with chlorine VCl_4 and with bromine and iodine VBr_3 and VI_2.

Even in the case of oxides which are normally capable of attaining the normal forms for which the degree of oxidation corresponds to the group number, we have a large number of exceptions. Thus the following solid and liquid oxides of the elements of Group VIII (iron and its analogs ruthenium and osmium) are known (substances which are metastable in the condensed state are indicated by asterisks:)

–	FeO*	Fe_3O_4	Fe_2O_3	–	–	–
–	–	–	$Ru_2O_3^*$	RuO_2	–	RuO_4^*
–	–	–	–	OsO_2	–	OsO_4

Only osmium gives a tetroxide OsO_4 corresponding to the group number and thermodynamically stable even under the conditions of distillation at 100°. The corresponding ruthenium compound RuO_4 decomposes explosively at a temperature of approximately 100°, liberating part of its oxygen and forming RuO_2. The highest thermodynamically stable oxide of iron at low temperatures is Fe_2O_3; the oxides corresponding to higher states of oxidation of iron are all unstable, are not found in the free state, and require for their stabilization the formation of complex compounds, for example, the ferrates.

TABLE 5

	Energy of formation (kcal.)	
	from the atoms	from simple substances
NO	—149	+21
$^1/_2\,N_2O_2$	—150.5	+20.5
$^1/_2\,N_2O_3$	—189.5	+10
NO_2	—221	+ 8
$^1/_2\,N_2O_4$	—227	+ 2
$^1/_2\,(N_2O_5)$	—256	+ 2.5
NO_3	—274.5	+17
$^1/_2\,Cl_2O$	— 47.5	+11
ClO	— 61	+27
$^1/_2\,Cl_2O_2$	— 62	+26
$^1/_2\,Cl_2O_3$	—110	+ 7.5
ClO_2	—121	+26
ClO_3	—179	+27
$^1/_2\,Cl_2O_6$	—180	+26
$^1/_2\,Cl_2O_7$	—204	+31.5
ClO_4	—200	+ 6.5

It is clear that the problem of the highest forms can be broken down to essentially two questions: one of these, which was solved at an early date by D.I. Mendeleev, is the question of the limiting forms possible from the viewpoint of the periodic law (normal forms); the other, which was also posed by D.I. Mendeleev, is the question of the forms which are attainable in practice and thermodynamically stable under ordinary conditions.

From the example just given, it follows that in the case of solid oxides, as in the case of gaseous substances, the low forms, as well as the high forms, are not always capable of existence. Thus osmium does not form Os_2O, OsO or Os_2O_3; ruthenium does not form Ru_2O or RuO, while the Ru_2O_3 described in the literature, prepared by careful dehydration of the corresponding hydroxide, is metastable at room temperature, like FeO, which, as is well known, is a substance capable of undergoing the reaction: $4FeO = Fe_3O_4 + Fe$ and which becomes truly stable only at temperatures above 570°.

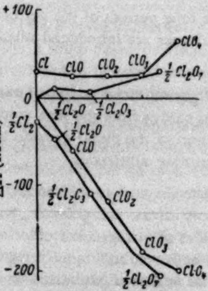

Fig. 5. The energies of formation of the oxides of chlorine from the free atoms (lower curves) and from the simple substances (upper curves).

The idea of the existence of two limits (an upper and a lower) in the series of stable compounds (for example, oxides) formed by an element has been particularly clearly formulated by A.A. Baikov [3], who by so doing took a further step in the development of the work of D.I. Mendeleev on per- and sub-compounds. As an illustration of the general applicability of this idea we give below lists of the oxides formed by the elements of the even series of periods IV - VI of the periodic system.

The asterisks denote metastable substances, while the vacant spaces correspond to compounds which are not found in practice in the free condensed state in macroscopic quantities. As can be seen from the data presented, whole series of both lower and higher oxides are so unstable that they are missing from the list of substances known to chemistry. In addition, in the case of certain elements gaps exist where different degrees of oxidation are missing within a series. Thus in the case of niobium Nb_2O_3 is missing, in the case of tantalum Ta_2O_3 and TaO_2, and in the case of osmium Os_2O_5, OsO_3 and Os_2O_7,* are missing.

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* In order to simplify the discussion at this stage we have not taken into account oxides of variable composition or oxides of intermediate type such as Mn_3O_4, Fe_3O_4, Co_3O_4, Pt_3O_4.

IV period

K_2O									
—	CaO								
—	—	Sc_2O_3							
—	TiO	Ti_2O_3	TiO_2						
—	VO	V_2O_3	VO_2	V_2O_5					
—	CrO^*	Cr_2O_3	CrO_2^*	$Cr_2O_5^*$	CrO_3^*				
—	MnO	Mn_2O_3	MnO_2	—	—	$Mn_2O_7^*$			
—	FeO^*	Fe_2O_3	—	—	—	—	—		
—	CoO	—	—	—	—	—	—	—	
—	NiO	—	—	—	—	—	—	—	—

V period

Rb_2O									
—	SrO								
—	—	Y_2O_3							
—	—	—	ZrO_2						
—	NbO	—	NbO_2	Nb_2O_5					
—	—	$Mo_2O_3^*$	MoO_2	Mo_2O_5	MoO_3				
—	—	—	TcO_2	—	TcO_3	Tc_2O_7			
—	—	$Ru_2O_3^*$	RuO_2	—	—	—	RuO_4^*		
—	—	Rh_2O_3	—	—	—	—	—	—	
—	PdO	—	—	—	—	—	—	—	—

VI period

Cs_2O									
—	BaO								
—	—	La_2O_3							
—	—	—	HfO_2						
—	TaO	—	—	Ta_2O_5					
—	—	—	WO_2	W_2O_5	WO_3				
—	—	—	ReO_2	—	ReO_3	Re_2O_7			
—	—	—	OsO_2	—	—	—	OsO_4		
—	—	—	IrO_2	—	—	—	—	—	
—	PtO^*	—	PtO_2^*	—	—	—	—	—	—

When we consider that the fact that these various oxides have not been found cannot, in the majority of cases, with the present-day position of science, be attributed to lack of study, chance failure, or the shortcomings of synthetic methods, it is natural to conclude that there exists a real law which prohibits the existence of certain compounds. The prohibition, of course, is not absolute, but is related in some fashion to the thermodynamic instability of the compounds in question, which is determined in turn by their specific chemical character. Attempts to explain the existence or nonexistence of various chemical compounds using thermodynamic theories and from the point of view of energy characteristics in particular, have been justified long ago, as is well known. We have only to recall the ideas put forward on this question approximately 30 years ago by Grimm [4], who calculated the approximate energies required for the formation of such imaginary compounds as the chlorides of the inert gases or nonexistent compounds such as $MgCl_3$, $AlCl_4$, etc.

Let us examine the oxides formed by the elements of the even series in the long periods of the periodic system, in order to find, on the basis of a concrete example, exactly what new features are introduced when we go from gaseous compounds to crystalline structures.

For the series of elements: K-Fe, Rb-Ru, Cs-Os, the somewhat schematic Figure 6 shows groups of curves, starting from the origin, and representing the energies of formation of the gaseous oxides from the free atoms; the curves starting from points corresponding to the energies of atomization of 1 g-atom of the metal provide information regarding the energies of formation of the same gaseous oxides from the simple substances.

If we examine Figure 6 in more detail, we see that the change from atoms to the simple substances, by raising the curves, causes a considerable number of the points (for example, almost all the points for Fe, Ru, and Os) to be transferred to the endothermic region, and this as in the case of the oxides of nitrogen and chlorine, is related principally to the high energies of sublimation of the metals; the curves, however, still remain regular, i.e., there is still no tendency for the saturation limit to be shifted from the normal degree of saturation to some other lower degree of saturation. Since the energies of sublimation of the metals increase considerably as we go from period IV to periods V and VI of the system, the field occupied by the figurative points in the endothermic region will be greatest in period VI.

For the sake of clarity we give below the values for the energies of atomization of the simple substances which we have used in the construction of Figure 6; all the values are calculated for 1 g-atom. The figures given

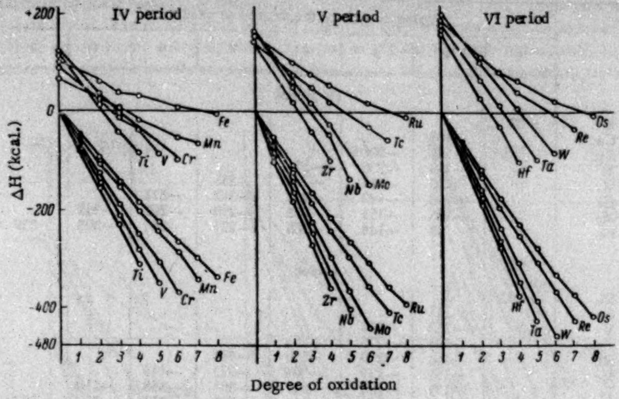

Fig. 6. The energies of formation of gaseous oxides (calculated for 1 g-atom of metal) from the free atoms (lower group of curves) and from the simple substances (upper group of lines).

in brackets are less reliable than the others, for which a number of new determinations have recently been made [2].

K	Ca	Sc	Ti	V	Cr	Mn	Fe
21.5	42.6	93	113	122	93	68	99
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru
20.5	39	(100)	142	162	156	(143)	(154)
Cs	Ba	La	Hf	Ta	W	Re	Os
19	42	88	(160)	(185)	202	189	174

Table 6 gives values for ΔH of formation of the gaseous molecules from the atoms, which we have also used [5] (in some cases for diatomic molecules spectral data are given, but in the majority of cases the values are calculated or interpolated using the thermal effects of oxide formation, from their heats of sublimation and from the energies of atomization of the simple substances).

We see from a comparison of the values of ΔH for periods IV, V and VI that Fig. 6 provides a good illustration of the periodicity which is a feature of the system of the elements. At the same time, in addition to the repetition in each period of similar geometrical characteristics, we also observe in the graphs a certain regularity in the course of the change in the quantitative expressions of these characteristics (which assists in interpolation). In effect, the original curves for ΔH for the gaseous oxides and atoms fall lower and lower as we change from period IV to period VI. Within the limits of the separate periods, we observe a lowering of the points on the same curves on going from the alkali metal to Cr, Mo and W, followed by a raising of the points after the elements of Group VI (according to a law governing movement along a horizontal row of the system, and not within a vertical column). Both these features are related to the interpretation of Bayley's rules [6], which were discussed by D.I. Mendeleev in his "Principles of Chemistry."

Figure 7 shows the change observed on going from the energies of formation of the gaseous oxides from the simple substances (upper curves) to the standard energies of formation of the solid oxides from the simple substances (lower curves), i.e., taking account of the energies of condensation.

As might have been expected, the curves showing the standard ΔH of formation in Fig. 7 lie below the original curves corresponding to the gaseous oxides, by virtue of the evolution of the energy of condensation.

TABLE 6

	Value of ΔH for the degree of oxidation							
	1	2	3	4	5	6	7	8
				IV period				
K	—39							
Ca		—104						
Sc		—138	—206.5					
Ti		—160	—236	—318				
V		—146	—217	—284	—355			
Cr		—130	—192	—252	—312	—371		
Mn		—106	—155	—203	—250	—297	—342	
Fe		— 98	—144	—186	—227	—267	—305	—339
				V period				
Rb	—29.5							
Sr		—111						
Y		—162	—243					
Zr		—184	—275	—365				
Nb		—168	—250	—330	—410			
Mo		—154	—229	—301	—373	—445		
Tc		—126	—186	—244	—301	—358	—410	
Ru		—112	—165	—216	—265	—313	—358	—397
				VI period				
Cs	— 9							
Ba		—126						
La		—161	—241.5					
Hf		—192	—277	—380				
Ta		—176	—263	—347	—431			
W		—160	—238	—314	—390	—465		
Re		—130	—193	—253	—313	—372	—430	
Os		—118	—174	—228	—282	—334	—376	—419

The most characteristic feature of the standard curves is the sharp change in their shape, which in the case of iron and manganese leads to the appearance of minima at the Fe_2O_3 and MnO_2 points, i.e., the highest, limiting, stable compounds.

To assist in a more detailed examination of Fig. 7, the numerical values for the data used in its construction [5] are given in Table 7.

Table 8 gives values for the energies of condensation of the oxides of the elements of periods IV-VI, although these values in a number of cases have no claim to accuracy, and in a number of cases even represent a certain degree of fiction, since by no means all of the oxides which are of interest to us (for example, oxides of the type M_2O_3 and M_2O_5) are stable in the gaseous state; some of them are polymerized in the vapor state.

Similarly Table 9 gives values for the energies of formation of the gaseous oxides from the simple substances.

When we examine the influence of the energy of condensation on the properties of the oxides, we should pay particular attention to the high values of these energies, which are often considerably greater than 100 kcal., i.e., they are reaching values of the same order as the energies of atomization of the solid metals. This fact is important not only in connection with the question of what it is that makes many endothermic gaseous oxides exothermic and stable in the solid state, but also in connection with the fact that the stabilization brought about by the energy of condensation often constitutes the whole or almost the whole of the exothermic effect of formation of the solid oxide. Thus, for example, if CaO were unable to form a crystalline structure at room temperature and were gaseous, its energy of formation would be of the order of -2 kcal.; the very high energy of condensation, equal to -150 kcal., is added to the -2 kcal., and gives a thermal effect of -152 kcal., as a result of which calcium oxide is very stable. The gaseous oxides MnO and FeO, which are characterized by endothermic formation effects equal to +21 and +60 kcal. respectively, might have behaved as explosive substances: they are in fact stabilized by their energies of condensation, equal to 113 and 123 kcal. Oxides such as UrO_2 and OsO_2 in the gaseous state would have endothermic heats of formation from the simple substances equal to +57 and +64 kcal., but their condensation energies, which are equal to 110 and 126 kcal. respectively, make them quite stable. The oxides of the alkali metals are likewise stable only by virtue of their condensed state.

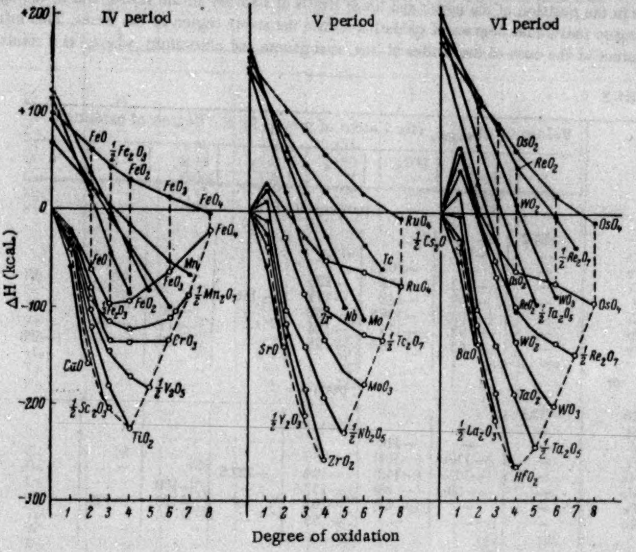

Fig. 7. The energies of formation of oxides (calculated for 1 g-atom of metal) from the simple substances.

Explanation in the text.

It is thus clear that the idea put forward persistently by D.I. Mendeleev, concerning the superposition of what were in the past called "physical" factors, for example, changes in states of aggregation, on purely chemical interactions, plays more than a secondary role in determining the fate and behavior of chemical compounds. It is of course not difficult to see what a decisive importance the energies of condensation will have in the formation of refractory and nonvolatile substances, such as the oxides, carbides, nitrides, etc.; more volatile compounds, the chlorides for example, will be dependent to a lesser extent on the condensation energies, but nevertheless these energies will play a part of no small importance in the case of the chlorides also.

It is also clear that the values of the condensation energies themselves depend on the structure of the crystals, on the change in coordination numbers on going from the molecules to the crystals, on the nature of the forces joining the atoms and ions, on the dimensions and polarizability of the atoms, and on many other factors, which are not always fully characterized by the term "physical" factor.

From a detailed examination of Table 8 we see that the smallest values of the quantity in question correspond to the 1st, 6th, 7th and 8th degrees of oxidation. A maximum condensation energy value, characteristic of the oxide series for a given element, is usually found to correspond to one of the degrees of oxidation lying between the 2nd and 4th. In periods V and VI this maximum is most often found to correspond to the 4th degree of oxidation; in period IV it is most often found to correspond to the 3rd degree of oxidation.

This phenomenon is evidently related to the particular features of the crystal structures of the individual chemical forms (M_2O_3, MO_2) and to the nature of the chemical bonds.

As a result of the existence of a maximum in the series of condensation energies corresponding to the different degrees of oxidation of a given element, the regular ΔH of formation curves for the gaseous oxides acquire important new features – minimum points and points of inflection (in the case of OsO_2, for example), which have an important influence on the chemical characteristics of the series of compounds. This influence is reflected both in the position of the upper and lower limits of stability in the series, and in the appearance of gaps corresponding to individual degrees of oxidation within the stable region of the series. This influence is particularly apparent in the case of the oxides of iron, manganese and chromium where, as a result of the low condensation energies, the oxides FeO_4, FeO_3, FeO_2, Mn_2O_7, MnO_3 are unstable and dissociate exothermically to form Fe_2O_3 and MnO_2; in the case of chromium, the oxide CrO_3 has the properties of a powerful oxidizing agent, while CrO_2 is a compound which is even difficult to prepare.

TABLE 7

	Values of $\Delta H_{stand.}$ (for 1 atom of metal) for the degree of oxidation							
	1	2	3	4	5	6	7	8
				IV period				
K	—43.2							
Ca	—	—152						
Sc	—	—	—205.5					
Ti	—	—122	—182	—226				
V	—	—103	—148	—171	—186			
Cr	—	(— 82)	—136.5	—138	—	—138		
Mn	—	— 92	—115	—124	—	(—111)	— 89	
Fe	—	— 63	— 98.5	— 95	—	(— 65)	—	(—25)
				V period				
Rb	—39.5							
Sr	—	—141						
Y	—	—	—210					
Zr	—	(—118)	(—185)	—259				
Nb	—	(—102)	(—142)	—194	—227.5			
Mo	—	(— 30)	(— 88)	—133.5	—	—180		
Tc	—	—	(— 67)	—103	—	—128	—133	
Ru	—	—	—	— 53	—	— 65	—	—77
				VI period				
Cs	—38							
Ba	—	—133						
La	—	—	—217.5					
Hf	—	(—119)	(—190)	—266				
Ta	—	(—101)	(—140)	(—190)	—244.5			
W	—	—	(— 68.5)	—136	—	—201		
Re	—	—	(— 49)	—102	—	—138	—148	
Os	—	—	—	— 62	—	— 75	—	—93.6

A study of Figure 7 enables us to understand the meaning of the Bayley rule, in which D.I. Mendeleev was interested. His "Principles of Chemistry" gives an example illustrating this rule, which states that the thermal stabilities of the highest oxides of the elements of the even series increase as we go from top to bottom of a vertical group in the periodic system; thus, WO_3 is more difficult to decompose by heating than MoO_3, which is in turn more stable than CrO_3.

The same rule is of course applicable to TiO_2, ZrO_2 and HfO_2; to Ta_2O_5, Nb_2O_5 and V_2O_5; to Re_2O_7, Tc_2O_7 and Mn_2O_7 and to OsO_4, RuO_4 and FeO_4.

The Bayley rule is illustrated in Fig. 7 by the sloping lines joining the points for the ΔH of formation of, for example, CrO_3, MoO_3 and WO_3.

It is now possible to characterize the Bayley rule [6] quantitatively and indicate the principle thermodynamic features which make it applicable; two such features can be recognized.

TABLE 8

	Values for energy of condensation (in kcal.) for degree of oxidation							
	1	2	3	4	5	6	7	8
				IV period				
K	54							
Ca	—	150						
Sc	—	—	182					
Ti	—	134	136	139				
V	—	138	142	130	100			
Cr	—	(104)	126	97	—	37		
Mn	—	113	117	107	—	(55)	21	
Fe	—	123	142	126	—	(74)	—	(21)
				V period				
Rb	56							
Sr	—	128						
Y	—	—	156					
Zr	—	(135)	(140)	154				
Nb	—	(155)	—	144	128			
Mo	—	(91)	(104)	107	—	68		
Tc	—	—	—	123	—	92	73	
Ru	—	—	—	110	—	83	—	70
				VI period				
Cs	58							
Ba	—	108						
La	—	—	153					
Hf	—	(146)	(161)	164				
Ta	—	(169)	(150)	—	147			
W	—	—	—	142	—	114		
Re	—	—	—	147	—	132	112	
Os	—	—	—	126	—	92	—	85

1) The increase [7] in the condensation energies of the highest oxides as we move down the system:

TiO_2	$^1/_2V_2O_5$	CrO_3	$^1/_2Mn_2O_7$	FeO_4
139	100	37	21	21
ZrO_2	$^1/_2Nb_2O_5$	MoO_3	$^1/_2Tc_2O_7$	RuO_4
154	128	68	73	70
HfO_2	$^1/_2Ta_2O_5$	WO_3	$^1/_2Re_2O_7$	OsO_4
164	147	114	112	85

This increase displaces the figurative points for the solid oxides in Fig. 7 downwards and makes the highest oxides more stable both relative to the lower oxides of the same element and also relative to the highest oxides of an element standing nearer the beginning of the system in the same vertical group.

2) The steeper shape of the bond energy curves for the gaseous molecules of elements situated low in the periodic system (this can be seen from Fig. 6); this shape results in compensation for the increase in the atomization energy of the metal, so that the points for FeO_4, RuO_4 and OsO_4, for example, on the ΔH of formation curves for the gases from the simple substances lie approximately on the same ordinate.

Science has still to reach a deeper understanding of the Bayley rule; indeed we still do not know just why the condensation energies in the series CrO_3, MoO_3, and WO_3 increase, and why they do so with such rapidity;

we likewise do not know why the bond energies in the gaseous molecules of the same substances, formed from the atoms, increase as we go from Cr to Mo and W.

TiO_2 —318	$^1/_2V_2O_5$ —355	CrO_3 —371	$^1/_2Mn_2O_7$ —342	FeO_4 —339
ZrO_2 —365	$^1/_2Nb_2O_5$ —410	MoO_3 —445	$^1/_2Tc_2O_7$ —410	RuO_4 —397
HfO_2 —380	$^1/_2Ta_2O_5$ —431	WO_3 —465	$^1/_2Re_2O_7$ —430	OsO_4 —419

Thus the shift of the upper limit in the oxide series for the period IV elements under discussion depends on the reduction in the condensation energies for high degrees of oxidation, while the nonappearance of this shift in the case of elements from periods V and VI is related to the less sharp change on going from the condensation energies for the 4th degree of oxidation to the energies for higher degrees of oxidation.*

TABLE 9

	Values for the energies of formation of gaseous oxides from the simple substances (in kcal.) for the degree of oxidation							
	1	2	3	4	5	6	7	8
				IV period				
K	+11							
Ca	—	— 2						
Sc	—	—	—24					
Ti	—	+ 12	—46	— 87				
V	—	+ 35	— 6	— 44	— 86			
Cr	—	+ 22	—10	— 41	—	—101		
Mn	—	+ 21	+ 2	— 17	—	— 56	—68	
Fe	—	+ 60	+43	+ 31	—	+ 9	—	—4
				V period				
Rb	+16							
Sr	—	— 13						
Y	—	— 5	—54					
Zr	—	+ 17	—45	—105				
Nb	—	+ 53	—	— 50	—100			
Mo	—	+ 61	+16	— 27	—	—112		
Tc	—	+ 76	+46	+ 19	—	— 36	—60	
Ru	—	+101	+77	+ 57	—	+ 18	—	—7
				VI period				
Cs	+20							
Ba	—	— 25						
La	—	— 14	—65					
Hf	—	+ 27	—29	—102				
Ta	—	+ 68	+10	—	— 98			
W	—	+101	—	+ 6	—	— 87		
Re	—	+118	+85	+ 45	—	— 6	—36	
Os	—	+115	+89	+ 64	—	+ 17	—	—9

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* It is undoubtedly true that the above-mentioned Bayley rules regarding the decrease in stability of the highest compounds of the elements in the odd series of the periodic system are related to the phenomenon of secondary periodicity.

It is now appropriate to consider the question of the rule relating to the shift of the lower limit. An examination of the list of stable oxides shows that the lower limit is shifted towards higher degrees of oxidation as we go from period IV to period V and even more as we go to period VI. Figure 7 reveals quite clearly the reason for this phenomenon: it is primarily due to the increase in the atomization energies of the metals, to the movement of ΔH, for many oxides corresponding to the 1st degree of oxidation, into the endothermic region (on the $\Delta H_{\text{stand.}}$ curves) and to the sharp approach of the remaining points corresponding to the 1st and 2nd, and sometimes also to the 3rd, degrees of oxidation, towards the zero ordinate, albeit in the exothermic region.

As a concrete example of this situation we may consider the oxides of osmium, of which only two are stable, OsO_2 and OsO_4 (Fig. 8). The lower oxides are not found as a result of the high atomization energy of osmium, and the consequent tendency for these oxides to break down exothermically to Os and OsO_2. The oxides intermediate between OsO_2 and OsO_4 also break down exothermically to form these two oxides. The reason for the phenomenon lies in the maximum value shown by the condensation energy of the oxide OsO_2.

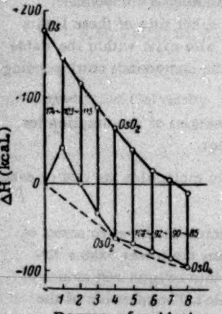

Fig. 8. The energies of formation of osmium oxides from the simple substances (upper curve for the gaseous oxides, lower curve for the condensed oxides).

Since the point for the compound Os_2O_3 lies above the straight line joining the OsO_2 point to the origin, Os_2O_3 is able to decompose exothermically to Os and OsO_2.

$$2Os_2O_3 - 54 = 3OsO_2 + Os$$

The particular favorable energy features of the OsO_2 crystal structure cause the point for this compound to be moved downward. If the line of points corresponding to the ΔH of formation for the gaseous oxides from the simple substances were not inclined so steeply as is actually the case for Os (period VI), but had a lower slope, like the lines for the oxides of iron (period IV), then the maximum condensation energy for OsO_2 might have resulted in the appearance of a minimum point on the ΔH curve for this oxide and thus determined the upper limit of the series. In the case of osmium, however, the minimum point for OsO_2 degenerates into a point of inflection: before OsO_2 the ΔH curve shows a convexity downward , while after OsO_2 it shows a convexity upward. As a result, the oxides intermediate between OsO_2 and OsO_4 have points which lie above the straight line joining the figurative OsO_3* and OsO_4 points; all these intermediate oxides therefore break down exothermically, for example

$$2OsO_3 - 6 = OsO_2 + OsO_4$$

Thus the particularly high condensation energy of OsO_2 leads, as it were, to the absorption by this compound of its neighbors in the series. It can be seen from this example that the importance of the heats of condensation of the oxides is considerable not only in connection with the shift of the upper limit of the series, but also in connection with the lower limit and the nonappearance of certain oxides within the series. In general the magnitude of the condensation energy of the free metal is reflected in a shift of the lower limit and in an overall reduction in the thermal stability of all the compounds of the element in question.

Thus the question of whether a given element, in combination with a second element, will give rise to few or many chemical forms (degrees of oxidation) depends not only on the number of electrons in the outer electron cloud of the atom (the number related to the group number of the element), but also on the chemical nature of the second element, or partner, on the energy of atomization, and sometimes also on the energy of ionization, of both partners, and also on the condensation energy of the compounds obtained. In resolving this problem of the stability of a particular form it is not at all sufficient to study that form in isolation: it is always necessary to study all the possible forms and the competition between them. In addition, of course, it is necessary to change from ΔH curves to ΔF curves, i.e., to take into account the values of $T\Delta S$. This can be readily done when the effect of temperature is taken into account.

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*As in original — Publisher's note.

It is undoubtedly true that, in solutions, the part of the condensation energy is taken by the solvation energies, by the energies of all the possible rearrangements in the structure of the molecules under study (precipitation, electrolytic dissociation, complex-formation, protolytic processes, polymerization, disproportionation), and also by the energy of the more intensive chemical processes taking place between the solvent and the dissolved substance (hydrolysis, the formation of oxy-ions, oxidation and reduction).

SUMMARY

1. The thermodynamic range of existence of a particular degree of oxidation for a given element depends on the statistical thermodynamic competition between the compound in question, the corresponding simple substances, and also the compounds of different degrees of oxidation, i.e., it is a characteristic which is necessarily dependent on the interrelationship between the members of the whole series of binary compounds which may be formed by the two simple substances.

2. The characteristic thermodynamic features of a series of stable compounds lead to the thesis that there exists an upper and a lower limit for the series, these limits corresponding to the formation of compounds saturated with the first or the second component; supersaturated compounds lying on either side of these limits disproportionate with the formation of the corresponding simple substance. Gaps may also exist within the stable limits, since individual states may break down by the exothermal decomposition of the compounds corresponding to these states into neighboring substances bordering the gap.

3. From an examination of the gaseous oxide series, it can be seen that high energies of atomization for the simple substances narrow the stability range in the oxide series for a given element.

4. In the breakdown of individual states of oxidation the question of whether the molecules are odd or even is significant, as is the phenomenon of polymerization of the compounds.

5. It has been shown that a considerable number of oxides formed by all the metals in the even series of the long periods of the periodic system are unstable in the gaseous state and dissociate: the lower oxides dissociate to the simple substances, while oxides of high degree of oxidation dissociate into oxygen and oxides of medium degree of oxidation (at high temperatures, where $T\Delta S$ plays an important role). The question of the gaseous oxides is complicated by the fact that in many cases we do not know the exact forms in which the various oxides exist in the vapor state.

6. In the case of the condensed oxides, an extremely important part is played by the enthalpies of condensation, which have maximum values for compounds of medium degrees of oxidation (4th or 5th degree in most cases). In period IV of the periodic system this feature in a number of cases leads to the formation of a minimum on the enthalpy curves, thereby creating conditions which lead to a reduction of the upper limit of stability to a state considerably lower than that corresponding to the group number. The fact that the decrease in the enthalpies of condensation of the highest oxides of the elements of periods V and, more especially, VI is less sharp than in period IV leads to the situation where the highest oxides of Tc, Ru, Re and Os are stabilized and there is then no minimum on the enthalpy of formation curves for the oxide series of these elements.

7. The well known Bayley rule concerning the shift of the upper limit of a series towards higher degrees of oxidation, i.e., the stabilization of the higher oxides, for d-metals, when we move from below upwards within the vertical groups of the periodic system, are explained in the light of the phenomena of the increase in the condensation energies of the highest oxides and the decrease in the endothermic effect of the gradual saturation of the metal atoms by oxygen.

8. A new rule has been pointed out concerning the shift of the lower limit in the series to higher degrees of oxidation as we move from above downwards within a group of the system. This rule is explained by the shape of the metal atomization energy curves.

9. In the region of the oxide with the highest condensation energy (for example, OsO_2), there arises a tendency for the neighboring oxides of higher and lower degrees of oxidation to disappear from the series as a result of disproportionation.

10. Analogous conclusions are also applicable to the explanation of the stability of individual degrees of oxidation in a wider sense, i.e., in the application of the above rules not only to oxides, but also to compounds of other types, and also to compounds in solution.

11. Certain analogies may also be pointed out with the characterization of the isotopic series of individual elements.

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Received March 11, 1957

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NUCLEAR (ATOMIC) CONCENTRATION AND SPECIFIC GRAVITIES OF HYDROCARBONS

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The value of the nuclear (atomic) concentration (NC) is determined by the total number of atoms of the original elements in the composition of a given substance, in a 1 liter volume,

$$NC = AN \text{ atoms} \tag{1}$$

where A is the nuclear concentration index and N is Avogadro's number.

In the case where the chemical formula of the substance has been determined (either rationally or empirically), the value of the nuclear concentration index is determined by the equation

$$A = 1000 \frac{nd}{M}, \tag{2}$$

where n is the number of atoms in a molecule, d is the specific gravity and M is the molecular weight.

We should note here that the value of the nuclear concentration index is very closely and obviously related to the concept of the average volume of an atom in complex bodies, introduced into science by D.I. Mendeleev [1]. The smaller the Mendeleev average atomic volume, the higher the value of A and the reverse.

In order to achieve a greater measure of objectivity the following calculations are based on literature data collected in one of the newest fundamental reference books [2].

If all the solid and liquid hydrocarbons listed in [2] which have been sufficiently investigated at a temperature as close as possible to + 20°, are sorted into groups by the increasing numbers of hydrogen atoms in the composition of one molecule, we will obtain a series of groups with the compositions C_XH_6, C_XH_8, C_XH_{10} etc. (Table).

Average Value of the Nuclear Concentration Index A_{av} of Hydrocarbons at + 20° According to Data in [2].

Formula	No. of compounds	A_{av}	Formula	No. of compounds	A_{av}
C_xH_6	14	128.1	C_xH_{20}	41	167.2
C_xH_8	26	137.7	C_xH_{22}	22	165.5
C_xH_{10}	63	145.5	C_xH_{24}	33	172.9
C_xH_{12}	87	151.3	C_xH_{26}	1	168.0
C_xH_{14}	109	155.6	C_xH_{28}	4	170.5
C_xH_{16}	153	161.4	C_xH_{30}	6	167.9
C_xH_{18}	89	164.6	C_xH_{32}	8	173.7

A full picture of the dispersion of separate points, corresponding to the calculated individual values of A for the separate members of a group may be drawn up for each of these groups and the value and character of the deviations from A_{av} that are observed may be evaluated quantitatively.

For this purpose we sorted all the 656 hydrocarbons, on which data is given in [2], into different groups and tabulated the data on the number of compounds in each separate group.

One may conclude from the data in this table that the average values calculated for the nuclear concentration index A_{av} and, consequently, the average values calculated for the nuclear concentration of hydrocarbons NC_{av}, increase smoothly and at a gradually decreasing rate with an increase in the number of hydrogen atoms in one molecule [3].

Then naturally a problem arises on the extent of dispersion of the A values and the number of substantial deviations from A_{av}. Of the 656 hydrocarbons, 610 compounds, or 93.0%, are characterized by values of the nuclear concentration index that differ by not more than 6% from the average values. Only 34 hydrocarbons, or 5.2% of the total number, have individual values for the nuclear concentration index A which exceed A_{av} by more than 6%. Five hydrocarbons in this group have unknown chemical structure while the remaining 29 compounds are either alicyclic compounds, i.e., are characterized by the presence of closed carbon atom chains, or are derivatives of naphthalene, anthracene and phenanthrene, i.e., they have condensed aromatic nuclei. Finally, 12 hydrocarbons, or 1.8% of the total number, are characterized by extremely low individual values for the nuclear concentration index. They are all unsaturated compounds of the aliphatic series.

In this way, an analysis of the factual material in [2] leads us to a second, important conclusion: at temperatures close to + 20° the great majority of hydrocarbons are characterized by values of the nuclear concentration index A that do not differ by more than 6% from the average calculated value of A_{av}. The relatively few deviations observed that were more than 6% over A_{av} have a regular character.

The temperatures at which the specific gravities given in [2] were determined are often far from + 20°. However, a difference of 10° in the temperature of liquid organic substances often causes a deviation of several percent in the nuclear concentration index A. Further, one should take into account the fact that the specific gravities given in the literature were determined by different experimenters at various times, by various methods and using preparations of differing origin and purity. Therefore, reference books often give specific gravities which differ by several percent even for the same substance at the same temperature. Finally, we are dealing here with two different aggregate states of material. At +20° about half of all the hydrocarbons given in [2] are in the liquid and the rest are in the solid state. Considering the above it is most remarkable that the great majority of the hydrocarbons described in the literature have values for nuclear concentration that fit within the rather rigid limits assigned by us.

The conclusions formulated above have more than theoretical interest. They may be applied in determining the molecular weights and chemical structures of hydrocarbons. Also this opens up the possibility of defining a regular relation between the composition and structure of hydrocarbons, on the one hand, and some of their chemical and physical properties, on the other. Let us consider the latter problem in more detail.

It follows from equation (2) that it is possible to establish unequivocally the specific gravity of any hydrocarbon of a given chemical composition if the value of its nuclear concentration index A is first known. Using the average values A_{av} given in the table for hydrocarbons containing from 6 to 32 hydrogen atoms in one molecule, we can establish by calculation the corresponding average specific gravities of all the diverse hydrocarbons with this composition, containing any number of carbon atoms, as found practically, in one molecule.

We calculated the average specific gravity at + 20° for a large number of hydrocarbons with the composition C_xH_z, where $\underline{x}$ varied from 2 to 26 and $\underline{z}$ from 6 to 32.

Of the total 656 hydrocarbons which, according to the data in [2], have this chemical composition, 618 compounds, or 94.2%, are characterized at + 20° by values of specific gravity which differ by not more than 0.05 from those calculated from A_{av}. Only 33 hydrocarbons (5.0%) have at 20° specific gravities which differ by 0.06 – 0.10 from the average value. Finally, only five hydrocarbons (0.8%) are given specific gravities in [2] which differ from the calculated specific gravities d_{av} by more than 0.10. The high values of specific gravity are characteristic of alicyclic hydrocarbons and hydrocarbons with condensed benzene nuclei. The low values of specific gravity are those of unsaturated compounds of the aliphatic series.

Thus, a study of the extensive factual material accumulated in the literature on hydrocarbons indicates that the combination of the observed nuclear concentrations and specific gravities of hydrocarbons may be represented in the form of a single, orderly system, which is closely related to the composition and structure of the substance.

SUMMARY

1. The value of the nuclear (atomic) concentration of solid and liquid substances (NC) is determined by the total number of atoms of the original elements, in the composition of the given substance, in a 1 liter volume.

2. The calculated average NC values of hydrocarbons increase regularly in the direction of greater numbers of hydrogen atoms in the composition of one molecule.

3. The great majority of hydrocarbons are characterized at temperatures close to + 20° by NC values which do not differ by more than 6% from the calculated average NC values. The deviations over 6% observed had a strictly regular character.

4. A study of extensive factual material indicated that not only the NC values, but also the specific gravities of hydrocarbons are closely related to their composition and structure.

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Received January 12, 1957

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THE VISCOSITY OF BINARY SYSTEMS WITH EXCHANGE INTERACTION

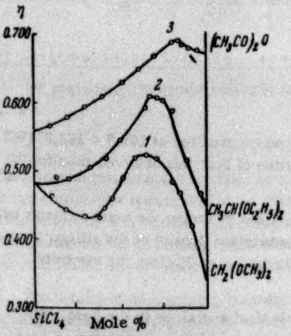
V.V. Udovenko and Iu.Ia. Fialkov

The viscosity diagrams of binary systems have been considerably systematized at the present time and are widely used for determining the character of the processes occurring. In the case of systems with chemical interaction, the existing classification [1] provides a type of diagram for systems in which the chemical reactions proceed with a decrease in the number of molecules, for example in the water – chloral system, or for systems in which the number of molecules remains the same, for example in the acetic anhydride – water system. As very few systems of the latter type have been studied, N.A. Trifonov proposed to investigate model systems such as diethyl ether – water, which could give an idea of the type of viscosity diagram for a system in which one chemical compound is formed without a change in the number of molecules.

It should be noted that in the acetic anhydride – water system the number of molecules does not change as a result of the chemical reaction as two molecules of acetic acid are formed from one molecule each of acetic anhydride and water. Reactions which proceed without a change in the number of molecules have possibilities other than the formation of only one chemical compound. Exchange interaction which results in two chemical compounds is not less widespread. This type of system is of considerable interest for the theory of physicochemical analysis but as yet no one has studied it by the viscosity method.

Data are given below on the viscosity of systems in which one of the components is silicon tetrachloride and the other is one of the following: methylal (dimethoxymethane), acetal (1,1-diethoxyethane) or acetic anhydride.

The silicon tetrachloride – methylal system



Viscosity isotherms at 20°
1. silicon tetrachloride – methylal
2. silicon tetrachloride – acetal
3. silicon tetrachloride – acetic anhydride, with benzene as solvent.

The silicon tetrachloride was purified in the same way as described in our previous work [2]. The procedure is also given there. Methylal was dried over potassium carbonate and distilled. The fraction with b.p. 41.5 – 42° (749 mm) was used in the work.

There was noticeable evolution of heat when silicon tetrachloride was combined with methylal. Measurements were taken a day after the mixture was prepared as the viscosity of the mixture changed for a certain period after the mixture was prepared. The experimental data on viscosity and density of this system at 20 and 30° are given in Table 1. The figure (curve 1) shows the viscosity isotherm of the silicon tetrachloride – methylal system at 20°. As the figure shows, the isotherm has a maximum in the region of 67 mole % of methylal which according to the generally accepted concepts on viscosity diagrams, should correspond to the formation of a molecular compound with a composition of 1 : 2. However, our previous investigations [2] had established that silicon tetrachloride did not form addition products with oxygen-containing organic substances. Consequently, the chemical reaction in this system is of a different character.

A mixture of silicon tetrachloride and methylal in a ratio of 1 : 2 was distilled at 745.5 mm. Two main fractions distilled off and these boiled at 59 – 61° and 98 – 100°. The analysis carried out gave the following results.

1st fraction. Found %: Cl 44.0. CH_3OCH_2Cl. Calculated %: Cl 44.04.

2nd fraction. Found %: Si 17.2; Cl 43.85. $SiCl_2(OCH_3)_2$. Calculated %: Si 17.4; Cl 44.04.

Thus, both the boiling points [4] and the results of analysis of the fractions indicate that the formation of dichlorodimethoxysilane and chlorodimethyl ether occurs in the system by the scheme

$$SiCl_4 + 2CH_2(OCH_3)_2 = SiCl_2(OCH_3)_2 + 2CH_3OCH_2Cl$$

In this case the maximum on the viscosity isotherm corresponds to the stoichiometric ratio at which the components react.

TABLE 1

The Viscosity and Density of the Silicon Tetrachloride – Methylal System

Methylal content (in mole %)	Density		Viscosity (in centipoises)	
	20°	30°	20°	30°
0.00	1.485	1.466	0.482	0.442
9.89	1.438	1.420	0.463	0.419
19.06	1.398	1.381	0.449	0.412
28.79	1.351	1.337	0.439	0.402
36.82	1.302	1.296	0.437	0.405
39.33	1.290	1.277	0.446	0.410
44.24	1.279	1.263	0.459	0.414
51.06	1.233	1.210	0.490	0.428
59.60	1.194	1.181	0.540	0.458
65.89	1.148	1.136	0.542	0.472
70.83	1.120	1.108	0.515	0.461
79.84	1.052	1.031	0.483	0.434
84.77	1.018	1.005	0.466	0.414
90.26	0.975	0.967	0.419	0.369
100.0	0.859	0.848	0.336	0.304

The silicon tetrachloride – acetal system

The acetal was purified in the same way as methylal. A fraction which distilled at 102.7 – 103.3° (747 mm) was used for the work. In preparing the mixtures noticeably more evolution of heat was observed than for the mixtures with methylal.

As the viscosity changed for a certain time after the preparation of the mixtures, the measurements were carried out a day after their preparation. The experimental data on viscosity and density of the silicon tetrachloride – acetal system at 20, 30 and 40° are given in Table 2. The figure (curve 2) gives the viscosity isotherm at 20°.

The viscosity isotherms have a maximum in the region of 67 mole % of acetal; as in the case with methylal, this maximum indicates the interaction of the components by the equation

$$SiCl_4 + 2CH_3CH(OC_2H_5)_2 = SiCl_2(OC_2H_5)_2 + 2C_2H_5OCH(Cl)CH_3$$

To confirm this scheme, we distilled a 1 : 2 mixture of silicon tetrachloride with acetal. The distillation gave two fractions: the 1st boiled at 96 – 98° and the second at 136°. An analysis of the fractions gave the following results.

1st fraction. Found %: Cl 32.4. $C_2H_5OCHClCH_3$. Calculated %: Cl 32.66.
2nd fraction. Found %: Si 14.2; Cl 37.4. $SiCl_2(OC_2H_5)_2$. Calculated %: Si 14.8; Cl 37.5.

Thus, the first fraction corresponded to α-chlorethyl ether and the second to dichlorodiethoxysilane [3].

It should be noted that phosphorus pentachloride reacts with acetal in an analogous manner. Bachmann [4] found that when phosphorus pentachloride was added in small portions to acetal, a reaction occurred by the scheme

$$CH_3CH(OC_2H_5)_2 + PCl_5 = C_2H_5OCH(Cl)CH_3 + C_2H_5Cl + POCl_3$$

The reactions of silicon tetrachloride with methylal, acetal and similar compounds may be of interest as an extremely convenient method for the directed synthesis of dichlorodialkoxysilanes, which proceeds in almost a 100% yield.

TABLE 2

Viscosity and Density of the Silicon Tetrachloride – Acetal System

Acetal content (in mole %)	Density			Viscosity (in centipoises)		
	20°	30°	40°	20°	30°	40°
0.00	1.485	1.466	1.447	0.482	0.462	0.402
13.00	1.393	1.377	1.361	0.489	0.450	0.410
20.26	1.342	1.326	1.311	0.488	0.450	0.413
32.44	1.251	1.236	1.220	0.503	0.459	0.421
41.02	1.199	1.185	1.171	0.515	0.475	0.427
49.27	1.147	1.135	1.121	0.542	0.492	0.442
59.09	1.092	1.081	1.067	0.572	0.515	0.461
63.77	1.062	1.050	1.039	0.591	0.534	0.476
67.03	1.044	1.032	1.021	0.609	0.538	0.484
71.00	1.024	1.012	1.008	0.606	0.552	0.490
74.57	0.998	0.987	0.976	0.600	0.541	0.481
80.82	0.958	0.948	0.938	0.586	0.520	0.467
83.85	0.949	0.938	0.928	0.555	0.492	0.447
88.13	0.913	0.903	0.891	0.514	0.456	0.410
96.55	0.855	0.845	0.835	0.465	0.416	0.375
100.0	0.837	0.827	0.817	0.451	0.404	0.364

The silicon tetrachloride – acetic anhydride system in benzene

We previously [5] established that when mixed silicon tetrachloride and acetic anhydride reacted by the equation

$$SiCl_4 + 4(CH_3CO)_2O = Si(OOCCH_3)_4 + 4CH_3COCl$$

to form silicon tetraacetate crystals. An exchange reaction also occurred in this system but it could not be studied as a two-component system due to the precipitation of crystals. Therefore, the silicon tetrachloride – acetic anhydride system was studied in benzene as an inert solvent. For this purpose we prepared solutions corresponding to an isoconcentrate containing 74.50 mole % of benzene. To complete the reaction, once prepared, the mixtures were sealed in tubes and heated on a boiling water bath for 1 hour.

The results of determining viscosity and density of the silicon tetrachloride – acetic anhydride system in solutions, containing 74.50 mole % of benzene at 20° are given in Table 3.

The viscosity isotherms are given in the figure (curve 3). As the figure shows, a rather sharp maximum is almost exactly at 80 mole % of acetic anhydride, i.e., exactly at the ratio at which the components react.

The examples we give show that in systems in which an exchange reaction is considerably displaced towards the formation of end products, the maximum on the viscosity isotherms indicates the stoichiometric ratio of the substances reacting. A series of factors may affect the position of the maximum in such systems, namely, the degree of the starting materials' reaction, their association, the relation of the viscosity magnitudes of all the substances participating in the reaction, etc. All these problems are being investigated further.

TABLE 3

Viscosity and Density of the Silicon Tetrachloride – Acetic Anhydride System in benzene at 20° (74.50 mole % of benzene isoconcentrate)

Acetic anhydride content (mole %)	Density	Viscosity (in centipoises)	Acetic anhydride content (mole %)	Density	Viscosity (in centipoises)
0.0	1.073	0.557	75.3	0.974	0.675
10.6	1.060	0.564	80.0	0.967	0.686
20.1	1.048	0.575	82.7	0.968	0.685
29.7	1.035	0.593	85.0	0.960	0.680
39.9	1.021	0.608	90.0	0.954	0.675
50.1	1.003	0.626	95.0	0.947	0.673
60.4	0.994	0.647	100.0	0.941	0.670
69.7	0.980	0.665			

SUMMARY

1. By means of the viscosity and density, we studied the binary systems silicon tetrachloride – methylal at 20 and 30°, silicon tetrachloride – acetal at 20, 30 and 40° and silicon tetrachloride – acetic anhydride in benzene, as an inert solvent, at 20°.

2. It was established that the maximum of the viscosity isotherms of systems in which an exchange reaction is considerably displaced towards the formation of end products, is at the stoichiometric ratio of the substances reacting.

3. It was established that silicon tetrachloride reacts with methylal to form dichlorodimethoxysilane and chlorodimethyl ether and it reacts with acetal to give dichlorodiethoxysilane and α-chlorodiethyl ether. These reactions are a new method for preparing dichlorodialkoxysilanes, which differs from existing methods in its high yield and purity of products.

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Received March 3, 1957

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PHYSICOCHEMICAL ANALYSIS OF BINARY SYSTEMS FORMED BY PHENOL WITH ACETIC ACID AND ITS CHLORO DERIVATIVES

I.M. Bokhovkin and E.G. Veselkova

As is known, the introduction of chlorine into an acetic acid radical results in increased acidity and, consequently, in greater chemical reactivity with other components [1]. This hypothesis was confirmed by studying binary systems formed by urea and acetamide with acetic acid and its chloro derivatives [2 - 6].

The purpose of the present work was to investigate the reaction of phenol with acetic acid and its chloro derivatives in the liquid phase.

The procedure has been described previously [2 - 6]. The starting materials were purified: acetic acid by freezing and phenol, monochloroacetic and trichloroacetic acids by distillation.

The concentrations are expressed in molecular percent, the surface tension in dynes/cm and the viscosity in centipoises. The surface tension, viscosity and density of all the systems were studied at 50, 70 and 90°.

The phenol – acetic acid system. The fusion diagram of the system consists of two branches of crystallization of the pure components, which cross at the eutectic point at 41.5% phenol and a temperature of -15° [7]. This form of diagram indicates the absence of chemical reaction in the system. The surface tension isotherms also indicate the same (Table 1, Fig. 1) as they increase smoothly from acetic acid to phenol; the density isotherms (Table 2, Fig. 2) are similar to an additive line; the viscosity isotherms (Table 3, Fig. 2) bulge towards the composition axis.

The phenol – monochloroacetic acid system was investigated by means of its fusion [8]. There was no chemical reaction of the components. The eutectic point corresponds to 69.0% phenol and 16.5°. The surface tension (Table 4, Fig. 3), density (Table 5, Fig. 4) and viscosity isotherms (Table 6, Fig. 4) also do not indicate the formation of a compound in the homogeneous, molten medium. The surface tension isotherms bulge towards the composition axis.

TABLE 1

Surface Tension of the Phenol – Acetic Acid System

C_6H_5OH (mole %)	Surface tension			C_6H_5OH (mole %)	Surface tension		
	50°	70°	90°		50°	70°	90°
0	24.46	21.79	20.04	39.6	30.43	27.75	25.45
5.9	25.23	22.21	20.69	44.3	31.13	28.40	26.11
10.6	25.99	23.40	21.35	49.6	31.77	29.12	26.85
14.9	26.63	24.05	21.98	54.8	32.59	29.81	27.58
20.0	27.56	24.85	22.76	59.1	33.00	30.45	28.12
24.4	28.15	25.47	23.45	64.8	33.87	31.05	28.79
31.7	29.26	26.58	24.37	70.0	—	31.61	29.35
36.0	29.96	27.19	24.99	75.0	—	—	29.98

TABLE 2

Density of the Acetic Acid – Phenol System

C_6H_5OH (mole %)	Density		
	50°	70°	90°
10	1.037	1.015	0.990
20	1.035	1.021	0.998
30	1.045	1.026	1.002
40	1.051	1.028	1.011
50	1.052	1.032	1.012
60	1.053	1.034	1.015
70	1.053	1.043	1.016

TABLE 3

Viscosity of the Acetic Acid – Phenol System

C_6H_5OH (mole %)	Viscosity		
	50°	70°	90°
10	0.84	0.60	0.44
20	1.03	0.69	0.50
30	1.22	0.79	0.55
40	1.44	0.89	0.62
50	1.69	1.01	0.67
60	1.97	1.14	0.74
70	2.29	1.29	0.81

In contrast to the preceding system, the surface tension hardly changes with changes in the mixture's composition.

The density decreases in the system from monochloroacetic acid to phenol. This decrease in density proceeds along an almost additive line. The viscosity of the system increases from monochloroacetic acid to phenol. The slope of the viscosity isotherm is less in this system than in the acetic acid – phenol system due to the small difference in the viscosities of monochloroacetic acid and phenol. It is also noteworthy that the viscosity of the monochloroacetic acid – phenol system decreases by a factor of approximately three with an increase in temperature from 50 to 90°.

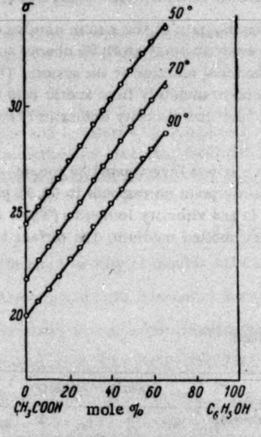

Fig. 1. Surface tension isotherms of the acetic acid – phenol system.

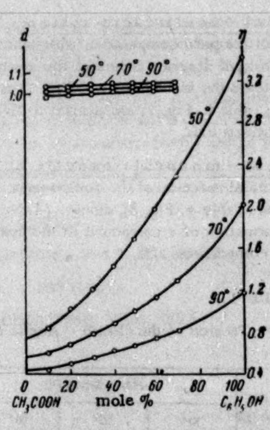

Fig. 2. Density (d) and viscosity (η) isotherms of the acetic acid – phenol system.

The phenol – trichloroacetic acid system. The chemical compound $C_6H_5OH \cdot CCl_3COOH$ was found in the system, which was studied by means of its fusion [8]. The fusion diagram shows this compound as a maximum (m.p. 37.50°). The surface tension (Table 7, Fig. 5) at 70 and 90° changes along an almost additive curve and increases smoothly from acetic acid to phenol. At 50° the isotherm deviates somewhat from

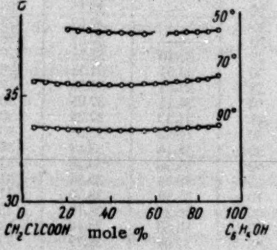

Fig. 3. Surface tension isotherms of the monochloroacetic acid – phenol system.

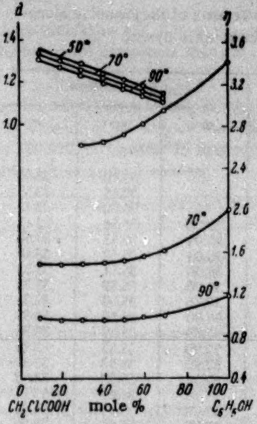

Fig. 4. Density (d) and viscosity (η) isotherms of the monochloroacetic acid – phenol system.

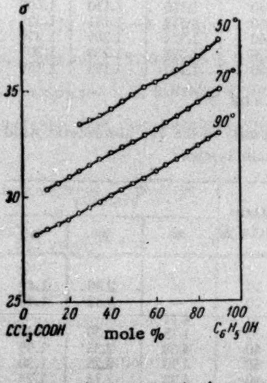

Fig. 5. Surface tension isotherms of the trichloroacetic acid – phenol system.

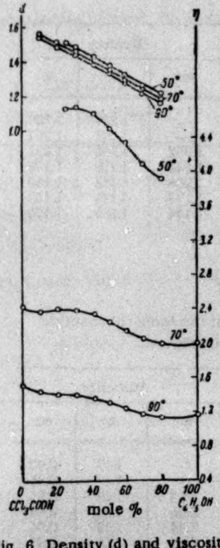

Fig. 6. Density (d) and viscosity (η) isotherms of the trichloroacetic acid – phenol system.

TABLE 4

Surface Tension of the Phenol – Monochloroacetic Acid System

C_6H_5OH (mole %)	Surface tension		
	50°	70°	90°
5	—	35.70	33.60
10	—	35.65	33.55
15	—	35.60	33.48
20	38.08	35.58	33.42
25	38.04	35.55	33.40
30	38.01	35.52	33.48
35	38.00	35.51	33.35
40	38.00	35.50	33.35
45	37.96	35.50	33.35
50	37.90	35.50	33.35
55	37.89	35.50	33.35
60	37.90	35.52	33.35
65	37.90	35.53	33.38
70	37.94	35.57	33.40
75	37.98	35.61	33.45
80	37.99	35.63	33.48
85	38.02	35.65	33.50
90	38.05	35.68	33.52

TABLE 5

Density of the Monochloroacetic Acid – Phenol System

C_6H_5OH (mole %)	Density		
	50°	70°	90°
10	—	1.339	1.309
20	—	1.301	1.267
30	1.282	1.256	1.231
40	1.244	1.219	1.196
50	1.208	1.182	1.168
60	1.177	1.154	1.133
70	1.144	1.120	1.108

TABLE 6

Viscosity of the Monochloroacetic acid – Phenol System

C_6H_5OH (mole %)	Viscosity		
	50°	70°	90°
10	—	1.49	0.97
20	—	1.49	0.95
30	2.63	1.48	0.95
40	2.66	1.50	0.95
50	2.74	1.52	0.96
60	2.84	1.56	0.97
70	2.96	1.62	0.99

TABLE 7

Surface Tension of the Phenol – Trichloroacetic acid system

C_6H_5OH (mole %)	Surface tension		
	50°	70°	90°
5	—	—	28.17
10	—	30.35	28.39
15	—	30.59	28.69
20	—	30.89	28.92
25	33.40	31.22	29.19
30	33.61	31.51	29.48
35	33.81	31.76	29.73
40	34.15	32.05	30.05
45	34.50	32.29	30.32
50	34.82	32.58	30.63
55	35.14	32.89	30.89
60	35.36	33.18	31.17
65	35.64	33.44	31.45
70	35.96	33.76	31.75
75	36.23	34.10	32.05
80	36.60	34.48	32.36
85	37.01	34.79	32.67
90	37.40	35.11	32.95

TABLE 8

Density of the Trichloroacetic Acid – Phenol System

C_6H_5OH (mole %)	Density		
	50°	70°	90°
10	—	1.562	1.541
20	—	1.511	1.486
25	1.508	—	—
30	1.477	1.458	1.435
40	1.426	1.410	1.382
50	1.373	1.351	1.328
60	1.324	1.289	1.270
70	1.253	1.238	1.207
80	1.207	1.175	1.150

TABLE 9

Viscosity of the Trichloroacetic Acid – Phenol System

C_6H_5OH (mole %)	Viscosity		
	50°	70°	90
10	—	2.39	1.45
20	—	2.42	1.42
25	4.74	—	—
30	4.75	2.39	1.40
40	4.68	2.35	1.35
50	4.50	2.25	1.30
60	4.33	2.14	1.24
70	4.07	2.05	1.17
80	3.91	1.95	1.13

the additive towards greater values of surface tension. The increase in surface tension seems to indicate the existence of the compound $C_6H_5OH \cdot CCl_3COOH$ in the molten state.

The density of the mixtures (Table 8, Fig. 6) decreases from trichloroacetic acid to phenol; the density isotherms almost coincide with the additive line and give no indication of component reaction in the homogeneous, molten medium.

The viscosity isotherms (Table 9, Fig. 6) are S-shaped curves. Such curves belong to systems with chemical reaction [8 - 10]. It is noteworthy that the viscosity decreases by a factor of 3.5 with an increase in temperature from 50 to 90°; the S-shape of the curves becomes increasingly less with an increase in temperature and this indicates considerable dissociation of the compound in the molten, homogeneous medium.

In comparing the surface tension, density and viscosity isotherms of all three systems studied, one can see that the introduction of chlorine into the acetic acid radical results in greater chemical reactivity between phenol and the acetic acid derivatives.

SUMMARY

1. Binary systems composed of phenol and acetic acid and its chloro derivatives were investigated physicochemically through their density, viscosity and surface tension.

2. The density, viscosity and surface tension isotherms of systems composed of acetic and monochloroacetic acids and phenol gave no indication of the existence of a compound in the molten medium.

3. The viscosity and surface tension isotherms and the fusion diagram of the trichloroacetic acid – phenol system indicate the existence of the compound $C_6H_5OH \cdot CCl_3COOH$.

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Received February 2, 1957

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INVESTIGATION OF CONTINUOUS TRANSITIONS FROM STABLE INTO METASTABLE PHASE SEPARATION

I.L. Krupatkin

The conversion of stable phase separation to the metastable state may be of practical interest as a method for obtaining alloys of two substances over the whole range of concentrations of the binary system formed by them. This problem is dealt with in a series of papers [1 - 4] in which the stable phase separation of a binary system is converted into a metastable state by adding a third component to it. It was shown that the continuous conversion that is described occurs in a ternary system through a cross section with a target and a point of contact of the fusion and phase separation curves. A series of basic forms of continuous conversions in the range of stable and metastable phase separation which may occur in ternary systems, as shown in Fig. 1 in the form of polythermal cross sections at mn of the prism of a ternary system A-B-C, may be derived for liquid phase equilibria with upper critical solution temperatures. Here, it is conditionally assumed that the A-B system is homogeneous in the liquid state, the A-C system has metastable phase separation and the B-C system has stable phase separation. The solid line on the cross sections b-e shows the polytherm of phase separation and the dotted line – the fusion polytherm of the A-B system (the fusion polytherm of the cross section mn may have the same form). The first form of the transition (b) is caused by a phase separation surface, without extreme and special points. The benzoic acid – salicylic acid – water system has this form of transition [1]. A transition of the second form (c) arises from a singular arm (point S lies on this arm). An example of this is the salicylic acid – picric acid – water system [2]. A transition of the third form (d) arises from the triple critical point K of the phase separation surface. This form of transition has not been achieved completely experimentally; a case that is very close to it, when the phase separation surface does not quite reach the boundary of the B-C binary system, occurs in the antipyrine – salicylic acid – water system [3]. The fourth transition form (e) arises from a saddle point F in the phase separation surface.

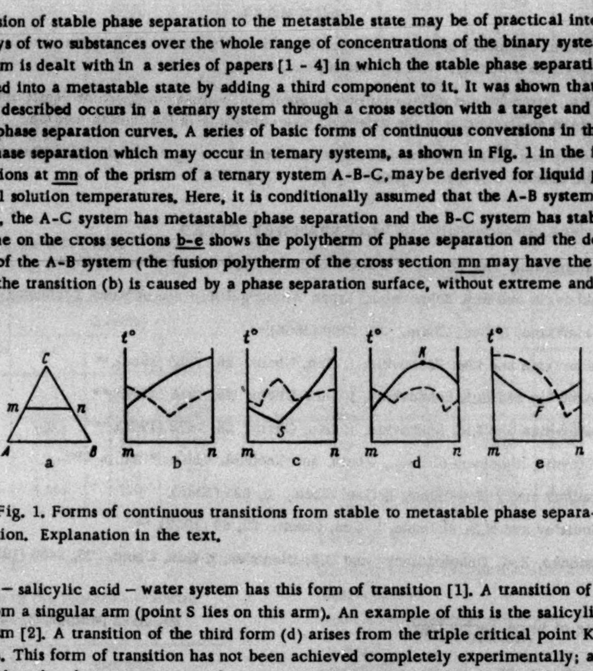

Fig. 1. Forms of continuous transitions from stable to metastable phase separation. Explanation in the text.

This transition form has not yet been found experimentally and its detection is the purpose of this work. The transition forms indicated may have various variants due to the changes in the character of geometric elements or changes in the relative position of the fusion and phase separation surfaces. Thus in case (c) the singular arm may be anticlinic, in cases c, d and e the singular arm and critical and saddle points may be either in the region of stable or metastable liquid phase equilibria.

EXPERIMENTAL

Salicylic acid – phenol – water and anthranilic acid – phenol – water ternary systems were used to achieve experimentally continuous reciprocal transitions from stable and metastable phase separation through a saddle point. The binary systems forming them were characterized by the following data. The phenol – water system was investigated by means of its fusion and phase separation [5]. The stable phase separation curve found has an upper critical point at 66°, which corresponds to 34% phenol; the monotectic equilibrium is at 12.2°. The salicylic acid – water system was investigated by means of its fusion and phase separation [6]. The metastable phase separation curve has an upper critical point at 89.1° (82% salicylic acid). The crystallization curve of the acid above the phase separation curve has a horizontal section at 104°. The anthranilic acid – water system was studied by means of its fusion and phase separation [7]. The upper critical point of the metastable phase separation curve at 78° corresponds to a 38% anthranilic acid content in the mixture. The crystallization curve of the anthranilic acid above the phase separation curve has a horizontal section at 105°. There is no data in the literature on systems formed by these acids and phenol. In the present work we attempted to investigate these systems by means of their fusion, though, due to the great viscosity of the mixtures of salicylic acid and phenol only part of the fusion diagram was studied and only separate points of the anthranilic acid – phenol system were obtained. The fusion curve of the first system did not indicate the formation of a compound. In spite of that, the tendency of the ortho derivatives of benzoic acid examined for complex formation suggested the formation of unstable complexes between them and phenol and this was confirmed by the present work. Thus, the presence of two binary systems with stable and metastable phase separation and a third with the formation of a dissociating complex in each of the ternary systems being studied made it possible to achieve transitions of the fourth form (d) in them.

TABLE 1

Equilibrium in the Salicylic Acid – Phenol System

Salicylic acid (weight %)	Crystallization temperature
26.85	76.0°
30.00	95.0
41.60	108.5
60.00	125.0
80.40	141.5
100.00	155.0

In the work we used the following substances: distilled phenol, a fraction boiling at 181° (m.p. 42°), salicylic and anthranilic acids of analytical purity with m.p. 155 and 145°, respectively, and doubly distilled water. The systems were investigated by means of their phase separation by the visual polythermal method of V.F. Alekseev [8] in sealed glass ampules in an oil thermostat. Investigation by means of their fusion was carried out by two methods in parallel – by Shreder's method [9] and by internal seeding [10].

The salicylic acid–phenol system was investigated by means of its fusion (Table 1, Fig. 2). The mixtures located close to phenol did not crystallize and, therefore, there is no data on them. Figure 2 shows that the crystallization curve of salicylic acid did not have either extreme or other special points.

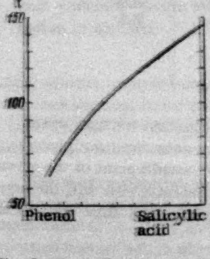

Fig. 2. Crystallization in the salicylic acid – phenol system

The salicylic acid – phenol – water[*] ternary system was studied by means of its phase separation (Table 2). Six polythermal cross sections of its temperature–concentration prism, going from the water arm to the boundary of the salicylic acid – phenol binary system were investigated (Table 2, Fig. 3). Figure 3 gives the fusion curve K_p and the phase separation curve P_a of the salicylic acid – water system and the phase separation curve aKb of the phenol – water system and the line of its monotectic equilibrium ab. As in the phase separation curves of binary systems, the reciprocal solubility polytherms of the liquid phases of a ternary system have upper critical solution temperatures. The latter descend from the critical points K and K_1 of phase-separating binary systems when the cross sections move into the prisms of ternary systems. Due to this, a saddle point forms on the phase separation surface of the ternary system between the fifth and sixth cross sections. It is found at 61.5° and a composition of 9% salicylic acid, 26% phenol and 65% water.

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[*] E.F. Leshchinskii participated in the investigation.

TABLE 2

Polytherms of the Salicylic Acid (SA) – Phenol (P) – Water System

Cross section 1: 20% P, 80% SA	
water (weight %)	phase separation temperature
33.00	50.0°
36.00	60.0
41.21	65.0
45.23	69.0
56.65	75.0
61.85	75.5
71.23	76.0
80.03	76.0
90.61	72.0
94.16	60.0
95.07	50.0

Cross section 2: 40% P, 60% SA	
water (weight %)	phase separation temperature
34.00	47.0°
40.00	58.0
45.00	63.0
52.00	67.0
61.70	81.5
70.00	69.0
80.42	69.0
90.73	64.0
94.50	47.0

Cross section 3: 50% P, 50% SA	
water (weight %)	phase separation temperature
34.50	47.5°
39.63	56.5
40.00	64.0
55.60	65.5
65.00	66.0
72.43	66.0
80.67	65.0
88.88	62.0
92.00	55.0
94.00	47.0

Cross section 4: 56.5% P, 43.5 % SA	
36.00	48.0°
40.65	57.0
52.51	63.0
63.50	65.0
67.72	65.0
69.04	65.0
80.86	64.0
91.32	56.0
93.06	51.5
94.00	46.0

Cross section 5: 60% P, 40% SA	
38.00	46.5°
41.55	52.5
48.00	60.0
51.64	62.5
60.42	63.0
67.37	63.0
71.87	63.0
80.14	62.5
91.39	54.0
92.94	48.0

Cross section 6: 80% P, 20% SA	
40.10	49.0°
45.00	55.0
50.96	59.0
60.03	62.0
70.43	62.0
80.02	61.0
85.00	55.0
90.04	48.0

The highest crystallization temperatures in the phase-separating mixtures of the cross sections are at 93, 84, 79, 74, 72 and 37° respectively in the 1, 2, 3, 4, 5 and 6 cross sections. These data show that phase separation is metastable in cross sections 1 – 5 and stable only in cross section 6. Thus, the saddle point of the given system should be located in the region of metastable liquid phase equilibria. In accordance with this, the crystallization surface, starting from the boundary of the salicylic acid – water system, must at first slope upwards but close to the boundary of the phenol – water system it will descend sharply.

Seven phase separation isotherms were plotted for the salicylic acid – phenol – water ternary system, given in Fig. 4, from the experimentally obtained polytherms. The isotherms at 85 - 62°, i.e., at high temperatures, limit phase separation into two separate regions which start at the solubility cross sections of the two binary systems. At 61.5° the phase separation regions abut on saddle point C. At 60 - 50°, i.e., at low temperatures, the isotherms form curves with reciprocal solubility maxima for the liquid phases. The isotherms maxima and the saddle point in the salicylic acid – phenol binary system are at 27% salicylic acid and 73% phenol. This composition corresponds to a complex with a 1:4 molecular ratio of these components. Consequently, the salicylic acid – phenol system is the dominating system in the ternary system being studied. The instability of the complex formed and its strong dissociation in water explain its greater solubility in water than those of its components and causes the formation of maxima on the phase separation isotherms and then the saddle point. An increase in the temperature intensifies these processes and results in a division of the phase separation region of the ternary system into two. In this way, a continuous transition of the stable phase separation of the phenol – water system into the metastable one of salicylic acid – water through a saddle point is achieved in the ternary system described (case e, Fig. 1).

Anthranilic acid – phenol – water ternary system. Table 3 gives the results of studying the polythermal cross sections through the temperature-concentration prism, going from the water arm to the boundary of the anthranilic acid – phenol binary system. Figure 5 shows the fusion curve K_p and the phase separation curve P_a of the anthranilic acid – water system and also the phase separation curve aKb and monotectic equilibrium line ab of the phenol – water system. The upper critical solution temperatures decrease from the critical points K and K_1 of the binary systems formed with water, as the cross sections move into the prism of the ternary system. Due to this a saddle point forms on the phase separation surface of the ternary system between the 3rd and 4th cross sections. This point is at 63.5° and corresponds to 10% anthranilic acid, 27% phenol and 63% water.

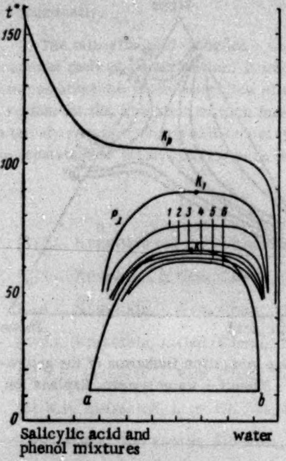

Fig. 3. Polytherms of the salicylic acid – phenol – water system. Explanation in the text.

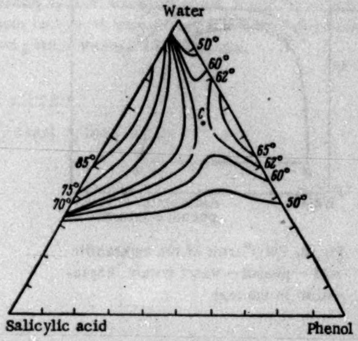

Fig. 4. Phase separation isotherms of the salicylic acid – phenol – water system. Explanation in the text.

Six phase separation isotherms of the anthranilic acid – phenol – water ternary system were plotted from the experimentally obtained polytherms and are shown in Fig. 6. The isotherms located above the saddle point (at temperatures of 73 - 64°) and the corresponding binary system conoids together limit to two the separate phase separation regions which abut on saddle point C at 63.5°. The isotherms located below the saddle point (at temperatures of 62 - 60°) are curves with maxima of reciprocal solubility of the liquid phases. The isotherm maxima and the saddle point in the anthranilic acid – phenol binary system are at 27% anthranilic acid and 73% phenol. This composition corresponds to a complex with a 1 : 4 molecular ratio. Consequently, the anthranilic acid – phenol system is the dominating system in the given ternary system. The formation of a complex in the dominating system and its decomposition in water explain the formation of the saddle point. Thus, continuous transition of a stable phase separation of the phenol – water system through a saddle point into the metastable one of the anthranilic acid – water system occurs in the anthranilic acid – phenol – water ternary system, i.e., case e, Fig. 1. It is interesting that in the dominating systems of both ternary systems studied a complex is formed with the same molecular ratio of the components. The great similarity of the phase separation diagrams of the ternary systems studied indicates that the properties of the two complexes are also analogous. This is explained by the similarity of the properties of the chemical components forming the complexes.

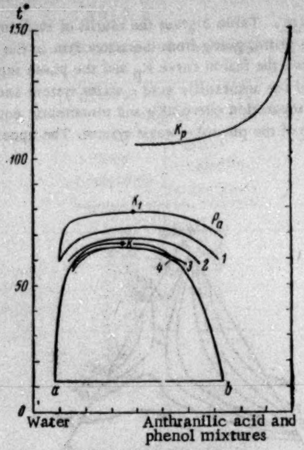

Fig. 5. Polytherms of the anthranilic acid – phenol – water system. Explanation in the text.

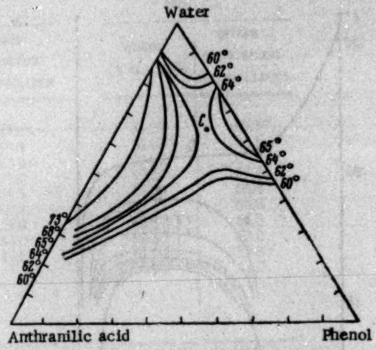

Fig. 6. Phase separation isotherms of the anthranilic acid – phenol – water system. Explanation in the text.

TABLE 3

Polytherms of the Anthranilic Acid (AA) – Phenol (P) – Water System

Cross section 1: 20% P, 80% AA	
water (weight %)	phase separation temperature
30.00	62.0°
40.00	69.0
51.00	72.5
60.00	73.0
70.00	71.0
80.00	69.0
90.00	59.0

Cross section 2: 40% P, 60 % AA	
water (weight %)	phase separation temperature
35.00	58.0°
40.00	63.0
50.00	66.5
60.00	68.5
70.00	67.0
80.00	65.5
85.00	61.0

Cross section 3: 60% P, 40% AA	
40.00	58.0°
48.00	63.0
56.00	64.0
60.00	64.0
70.00	64.0
80.00	62.0
85.00	56.5

Cross section 4: 80% P, 20% AA	
43.00	58.0°
50.00	62.0
60.00	64.5
70.00	64.5
80.00	61.0
85.00	55.0

SUMMARY

1. The forms of continuous reciprocal transitions of metastable and stable phase separation of binary and ternary systems were examined. They were reduced to four basic types.

2. The components of the salicylic acid – phenol binary system, studied by means of its fusion, did not react chemically.

3. The salicylic acid – phenol – water and anthranilic acid – phenol – water ternary systems were studied by means of their phase separation. It was found that in both cases the phase separation volume of the ternary system combines the phase separation planes of the two binary systems formed with water and has a saddle point. The reasons for the formation of such forms of diagram for ternary systems were explained. It was shown that in both ternary systems investigated one of the forms of continuous reciprocal transition of metastable and stable phase separation of binary systems occurred with this transition passing through a saddle point.

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Received January 12, 1957

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TERNARY RECIPROCAL SYSTEM OF LITHIUM AND SODIUM FORMATES AND NITRATES

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The system of lithium and sodium formates and nitrates is the first to be investigated in the systematic study of systems of lithium salts of aliphatic acids and lithium and sodium nitrates.

Work carried out by A.G. Bergman et al. [1] showed that in some systems with lithium salts, the direction of the exchange reaction does not correspond to its conventional thermochemical effect; this makes the study of systems with lithium salts much more interesting.

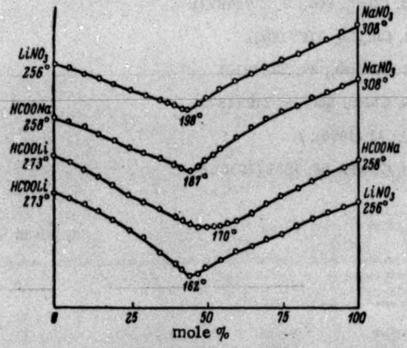

Fig. 1. Fusion curves of binary systems

A visual polythermal method was used for the investigation. The temperature was measured with a nichrome-constantan thermocouple. The fusion was carried out in a test tube which was placed in a larger test tube for even heating. The melts were mixed manually with a glass mixer. The calibration curve was plotted from the boiling point of water and the melting points of benzoic acid (122.5°), mannitol (166°), succinic acid (183°), sodium nitrate (308°) and potassium nitrate (337°). Analytically pure grades of salt were purified by 2 recrystallizations. The melting points of the salts were: 308° for sodium nitrate, 256° for lithium nitrate and 258° for sodium formate. The lithium formate decomposed when heated and its melting point was determined by extrapolation using the binary systems: lithium formate – sodium formate and lithium nitrate – lithium formate. It was found to be 273°.

According to the literature data, polymorphous conversions are known for sodium nitrate at 275° [2] and sodium formate at 242° [3]. The composition is expressed everywhere in molar percent.

Binary systems. According to data in [4] the sodium nitrate – lithium nitrate system forms a continuous series of solid solutions. According to later data [5], the system has a eutectic containing 41.5% $NaNO_3$ with m.p. 195° or, according to data [6], 43.75% sodium nitrate with m.p. 196°. According to our data, the eutectic point corresponds to 45% $NaNO_3$ and 198°.

TABLE 1

Binary Systems

$LiNO_3$—$NaNO_3$		$LiNO_3$—HCOOLi		HCOOLi—HCOONa		HCOONa—$NaNO_3$	
mole % $NaNO_3$	temperature	mole % HCOOLi	temperature	mole % HCOOLi	temperature	mole % $NaNO_3$	temperature
0	256°	0	256°	0	258°	0	258°
5	250	5	247	5	250	5	252
10	242	10	238	10	242	10	245
15	236	15	228	15	232	15	236
20	230	20	220	20	224	20	226
25	224	25	212	25	214	25	219
30	216	30	206	30	204	30	212
35	210	35	196	35	194	35	204
40	204	40	188	40	182	40	196
45	198	45	180	45	176	45	188
50	208	50	170	50	170	50	192
55	219	55	162	55	175	55	210
60	230	60	178	60	184	60	226
65	240	65	194	65	196	65	240
70	250	70	208	70	208	70	250
75	260	75	220	75	220	75	260
80	270	80	232	80	232	80	270
85	280					85	278
90	290					90	288
95	300					95	298
100	308					100	308

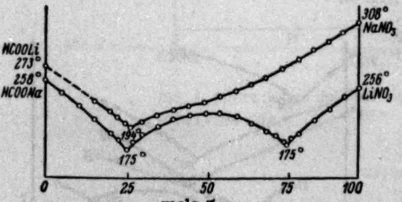

Fig. 2. Diagonal cross sections of the ternary reciprocal system.

The lithium nitrate – lithium formate system was first investigated by us. The eutectic point corresponds to 55% lithium formate and 162°. The system was studied up to 80% lithium formate.

The sodium formate – lithium formate system was first investigated by N.M. Sokolov [3]. According to our data, the system forms solid solutions at a minimum m.p. of 170° at 50% sodium formate.

According to our measurements the sodium nitrate – sodium formate system [3] has a eutectic containing 48% sodium nitrate with m.p. 187° (Table 1, Fig. 1).

Diagonal cross sections. The sodium formate – lithium nitrate diagonal cross section is not stable. The branches of the first crystals of the components go down to 175° and intersect the branch of the exchange product in two eutectic points at 24 and 76% lithium nitrate.

The sodium nitrate – lithium formate diagonal cross section was studied up to an 80% lithium formate content. In the section studied, its diagram consists of two branches which intersect at the eutectic point at 194° and 26% sodium nitrate (Table 2, Fig. 2). We consider this diagonal cross section to be stable.

Internal cross sections. The internal cross sections were studied to find the limits of the fields of first crystallization. The directions of the cross sections are shown in Fig. 3 and their characteristics are given in Fig. 4.

TABLE 2

Diagonal Cross Sections

$LiNO_3$–HCOONa				$NaNO_3$–HCOOLi			
mole % HCOONa	temperature	mole % HCOONa	temperature	mole % $NaNO_3$	temperature	mole % $NaNO_3$	temperature
0	256°	55	220°	20	225°	60	235°
5	245	60	215	25	196	65	242
10	230	65	208	26	194	70	246
15	212	70	190	30	197	75	254
20	194	75	175	35	204	80	264
24	175	80	192	40	208	85	272
25	180	85	210	45	215	90	284
30	196	90	230	50	222	95	294
35	204	95	242	55	228	100	308
40	214	100	258				
45	220						
50	222						

A stable diagonal cross section divides the square of the system into two phase triangles: 1) lithium nitrate – sodium nitrate – lithium formate and 2) sodium nitrate – sodium formate – lithium formate. The first phase triangle has a triple point at 146°, 14% sodium nitrate, 46% lithium nitrate and 40% lithium formate. In the second phase triangle the triple point lies at 154°, 14% sodium nitrate, 49% lithium formate and 37% sodium formate.

The diagram of the ternary reciprocal system has five crystallization fields. The areas of these fields (in percent of the total area of the square) consist of: sodium nitrate 57.13, lithium formate 13.92, lithium nitrate 13.80, sodium formate 12.16; 3% is taken up by the field of the HCOOLi – HCOONa solid solutions, which decompose when more than 5% of a third component is added.

The results of the experimental data are generalized in the form of isotherm projections on the square of the system (Fig. 5). The positions of invariant points and cocrystallization lines are given in the form of the projection of these points on the HCOOLi – HCOONa side (Fig. 6).

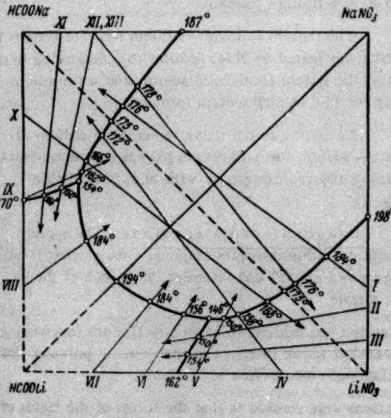

Fig. 3. The direction of internal cross sections

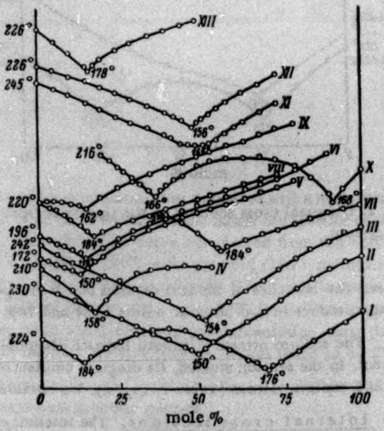

Fig. 4. Characteristics of the internal cross sections

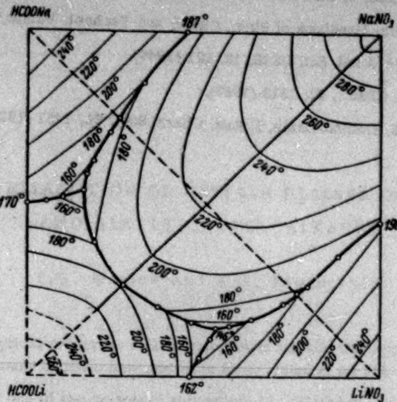

Fig. 5. Projection of the reciprocal system diagram on the composition square.

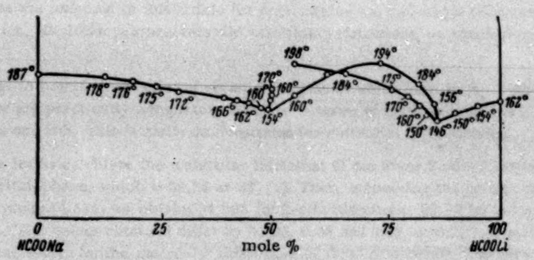

Fig. 6. Projection of the cocrystallization line on the HCOOLi – – HCOONa side.

SUMMARY

1. The ternary reciprocal system of lithium and sodium formates and nitrates was investigated by a visual polythermal method and, according to the classification of A.G. Bergman and N.S. Dombrovskaia [7], this system is an irreversible reciprocal system.

2. The chemical exchange equilibrium in the system is displaced toward lithium formate and sodium nitrate, which are the most refractory of the system's components.

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Received December 14, 1956

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THE MOLECULAR REFRACTION OF CERTAIN CLASSES OF ALKYLTHIOPHENES AND ALKYLTHIACYCLOALKANES

P.G. Maslov and A.A. Klochikhin

A knowledge of the physical properties of alkylthiophenes and alkylthiacycloalkanes is of great value practically. In spite of this, many of them have not been investigated at all [1].

A method, proposed by one of the authors of this article [2 - 7] makes it possible to fill in this gap rapidly.

In previous reports [8] a general formula was proposed for determining the standard molar specific heats, entropies and heats of formation of gaseous and liquid 3-thiaalkanes, 2-thiaalkanes, 1-alkanethiols and 3,4-dithiaalkanes.

Single formulas are proposed in this article for determining the molecular refraction R_D of alkylthiophenes, alkylthiacyclopropanes, alkylthiacyclopentanes and alkylthiacyclohexanes, on which there is no data in the literature [1].

It is known that in homologous series of organic compounds which form a ring (cylopentane, cyclopropane etc), many properties are practically completely additive in terms of methylene groups (CH_2) from the second member of the series onwards. This is easily demonstrated for molecular refraction R_D.

As an example let us calculate the molecular refraction of the lower 2-alkylthiophenes from the molecular refraction of 2-propylthiophene, which is 38.64 at 20° [1]. Then, subtracting the portion of R_D that may be assigned to one CH_2 group (4.635) we obtain: 34.005 for 2-ethylthiophene, 29.37 for 2-methylthiophene and 24.735 for thiophene. The values obtained differ by 0.095, 0.08 and 0.37, or 0.3, 0.25 and 1.5%, respectively from the experimental values for the molecular refractions of these compounds. This shows that as one proceeds further from the beginning of the 2-alkylthiophene series, the deviation from additivity decreases rapidly and that of the third member is only 0.095 or 0.3%. One naturally expects practically complete additivity starting from 2-butylthiophene. A check shows that the same situation occurs in 3-alkylthiophenes, alkylthiacycloalkanes and others. Using the values given in [1] for the molecular refraction of the third and especially the fourth member of an homologous series of organosulfur compounds, this makes it possible to obtain general rules for determination of the R_D of all the other members of the particular series of compounds (with the exception of the starting members).

Analyzing the molecular refraction, R_D, of some alkylthiophenes and alkylthiacycloalkanes given in [1] using the above method, we found the following general formulas for determining molecular refractions R_D.

2-Alkylthiophenes and 3-alkylthiophenes:

$$R_D = 24.735 - 0.06\,(r - 1) + 4.635 \cdot z \text{ at } 20^\circ \; (z \geq 1) \tag{1}$$

$$R_D = 24.755 - 0.06\,(r - 1) + 4.635 \cdot z \text{ at } 25^\circ \; (z \geq 1) \tag{2}$$

2-Isoalkyl- and 3-isoalkylthiophenes:

$$R_D = 24.705 - 0.13\,(r - 1) + 4.635 \cdot z \text{ at } 20^\circ \; (z \geq 1) \tag{3}$$

$$R_D = 24.715 - 0.13\,(r - 1) + 4.635 \cdot z \text{ at } 25^\circ \; (z \geq 1) \tag{4}$$

TABLE 1

Molecular Refractions of Some Alkylthiophenes and Alkylthiacyclopropanes

Name of alkylthiophene	Chemical formula	20°			Name of alkylthiacyclopropane	Chemical formula	20°		
		calculated by formulas (1) - (4)	data from [1]	Δ			calculated by formula (9)	data from [1]	Δ
Thiophene	C_4H_4S	24.735	24.365	+ 0.37	Thiacyclopropane	C_2H_4S	17.33	17.2	+ 0.13
2-Methylthiophene.	C_5H_6S	29.37	29.29	+ 0.08	2-Methylthiacyclopropane. . . .	C_3H_6S	21.96	22.1	− 0.14
2-Ethylthiophene	C_6H_8S	34.00	33.91	+ 0.09	2-Ethylthiacyclopropane.	C_4H_8S	22.60	26.6	0.0
2-Propylthiophene	$C_7H_{10}S$	38.64	38.64	0.00	2-Butylthiacyclopropane.	$C_5H_{10}S$	31.24		
2-Butylthiophene	$C_8H_{12}S$	43.28			2-Pentylthiacyclopropane	$C_6H_{12}S$	35.87		
2-Pentylthiophene etc.	$C_9H_{14}S$	47.91			2-Hexylthiacyclopropane	$C_7H_{14}S$	40.50		
3-Methylthiophene.	C_5H_6S	29.31	29.225	+ 0.095	2-Heptylthiacyclopropane. . . .	$C_8H_{16}S$	45.14		
3-Ethylthiophene.	C_6H_8S	33.94	33.88	+ 0.06	2-Octylthiacyclopropane.	$C_9H_{18}S$	49.78		
3-Propylthiophene	$C_7H_{10}S$	38.58	38.58	0.00	2-Nonylthiacyclopropane etc. .	$C_{10}H_{20}S$	54.11		
3-Butylthiophene.	$C_8H_{12}S$	43.22							
3-Pentylthiophene	$C_9H_{14}S$	47.85							
3-Hexylthiophene etc	$C_{10}H_{16}S$	52.48							
2-Isopropylthiophene etc. . .	$C_7H_{10}S$	38.61	38.61	0.00					
Per CH_2 group . .		4.635			Per CH_2 group .		4.635		

TABLE 2

Molecular Refractions of Some Alkylthiacyclohexanes and Alkylthiacyclopentanes

Name of alkylthiacyclohexane	Chemical formula	20°			Name of alkylthiacyclopentane	Chemical formula	20°		
		calculated by formula (5)	data from [1]	Δ			calculated by formula (7)	data from [1]	Δ
2-Methylthiacyclohexane . . .	$C_6H_{12}S$	35.67	35.67	0.00	Thiacyclopentane	C_4H_8S	26.330	26.179	+ 0.121
3-Methylthiacyclohexane . . .	$C_6H_{12}S$	35.62	35.61	+ 0.01	2-Methylthiacyclopentane . . .	$C_5H_{10}S$	30.965	30.98	− 0.015
4-Methylthiacyclohexane . . .	$C_6H_{12}S$	35.57	35.62	− 0.05	3-Methylthiacyclopentane . . .	$C_5H_{10}S$	30.765	30.80	− 0.035
2-Ethylthiacyclohexane.	$C_7H_{14}S$	40.30			2-Ethylthiacyclopentane.	$C_6H_{12}S$	35.60	35.6	0.0
3-Ethylthiacyclohexane.	$C_7H_{14}S$	40.26			3-Ethylthiacyclopentane.	$C_6H_{12}S$	35.40	35.4	0.0
4-Ethylthiacyclohexane.	$C_7H_{14}S$	40.20			2-Propylthiacyclopentane	$C_7H_{14}S$	40.24		
2-Propylthiacyclohexane. . . .	$C_8H_{16}S$	44.94			3-Propylthiacyclopentane	$C_7H_{14}S$	40.04		
3-Propylthiacyclohexane. . . .	$C_8H_{16}S$	44.89			2-Butylthiacyclopentane.	$C_8H_{16}S$	44.87		
2-Butylthiacyclohexane.	$C_9H_{18}S$	49.58			3-Butylthiacyclopentane.	$C_8H_{16}S$	44.67		
3-Butylthiacyclohexane.	$C_9H_{18}S$	49.52			2-Pentylthiacyclopentane	$C_9H_{18}S$	49.50		
2-Pentylthiacyclohexane etc .	$C_{10}H_{20}S$	54.21			3-Pentylthiacyclopentane	$C_9H_{18}S$	49.30		
					2-Hexylthiacyclopentane etc. .	$C_{10}H_{20}S$	54.14		
Per CH_2 group . .		4.635			Per CH_2 group . .		4.635		

2-Alkyl-, 3-alkyl- and 4-alkylthiacyclohexanes:

$$R_D = 31.035 - 0.05\,(r-1) + 4.635 \cdot z \text{ at } 20° \ (z \geq 1) \tag{5}$$

$$R_D = 31.045 - 0.05\,(r-1) + 4.635 \cdot z \text{ at } 25° \ (z \geq 1) \tag{6}$$

2-Alkyl- and 3-alkylthiacyclopentanes:

$$R_D = 26.33 - 0.2\,(r-1) + 4.635 \cdot z \text{ at } 20° \ (z \geq 1) \tag{7}$$

$$R_D = 26.343 - 0.113\,(r-1) + 4.635 \cdot z \text{ at } 25° \ (z \geq 1) \tag{8}$$

2-Alkylthiacyclopropanes:

$$R_D = 17.33 + 4.635 \cdot z \quad \text{at } 20° \ (z \geq 1) \tag{9}$$

$$R_D = 17.34 + 4.635 \cdot z \quad \text{at } 25° \ (z \geq 1) \tag{10}$$

In formulas (1) - (10) z is the number of methylene groups or carbon atoms in the linear carbon chain C-C-C. . . of a molecule of the appropriate compound; r is the number of carbon atoms in the ring from which the C-C-C chain starts.

The reliability of the results depends on the accuracy of the molar refraction values for 2- and 3-propylthiophene, 2-, 3- and 4-ethylthiacyclohexanes and 2- and 3-ethylthiacyclopentanes, taken from [1] and used for deriving the equations given above. However, if it is found later that the initial values are greater than the true ones by a term δ, this may readily be taken into account in formulas (1) - (10) by adding δ to the first term in the right section. Furthermore, the accuracy of the formulas depends on the amount the initial value of R_D of 2-propylthiophene and others is less than its additive value. The error, due to this reason, is not greater than 0.2 – 0.3%.

In Tables 1 and 2 are given the molecular refractions at 20° for a series of alkylthiophenes and alkylthiacycloalkanes. Most of them are presented for the first time. Some of them are compared with the existing literature data found in [1]. As can be seen, the values of molecular refractions calculated by our formulas agree very well with the experimental data.

SUMMARY

1. General formulas are derived for determining the values of molecular refractions, R_D, at 20 and 25° for 2-alkylthiophenes, 3-alkylthiophenes, 2-isoalkylthiophenes and 3-isoalkylthiophenes, with an accuracy of the order of 0.2 – 0.3% if one considers the data in [1] as correct.

2. General formulas are proposed for determining the values of molecular refraction, R_D, at 20 and 25° for 2-alkyl-, 3-alkylthiacyclopentanes, for 2-alkyl-, 3-alkyl- and 4-alkylthiacyclohexanes and for 2-alkyl- and 3-alkylthiacyclopropanes. The accuracy is of the order of 0.2 – 0.3%, if the initial data in [1] are considered correct.

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Received July 10, 1956

** Original Russian pagination. See C.B. Translation.

DISCUSSION

CONCERNING THE PAPERS OF L.M. LITVINENKO, R.S. CHESHKO, S.V. TSUKERMAN, A.D. GOFMAN, B.M. KOLESNIKOVA AND OTHERS ON "SPATIAL STRUCTURE AND REACTIVITY"

E.N. Gur'ianova

A series of papers [1 - 3] under the title of "Spatial Structure and Reactivity" was published in Vol. 27 of the Journal of General Chemistry.

The objective of the authors was to solve the extremely topical problem of the transmission of the reciprocal effects in molecules with conjugated bonds across atoms of oxygen, sulfur, etc., included in the conjugated system. The rate of acylation of 4-aminobiphenyl, 4-aminodiphenyl oxide, 4-aminodiphenyl sulfide and their 4'-derivatives was measured in these investigations, using 4-nitrobenzoyl chloride as the acylating agent. It was shown that the introduction of a nitro group in the 4'-position of the compounds in question considerably slowed down the acylation process, and the magnitude of this retarding effect decreased in the following order: diphenyl sulfide > diphenyl oxide > biphenyl.

On the basis of these facts the authors inferred that the molecular systems of diphenyl oxide and diphenyl sulfide are – in spite of the oxygen and sulfur bridges between their benzene rings – better transmitters of the electronic interaction of the substituents than the biphenyl system in which these rings are directly linked. This conclusion is not adequately proven.

In considering the experimental data, the authors did not take into account the differences in the spatial configuration of biphenyl derivatives (linear) on the one hand and that of diphenyl oxide and diphenyl sulfide (angular) on the other. Moreover, the considerable drop in the rate of reactions in 4'-nitro derivatives in comparison with unsubstituted compounds in the case of diphenyl oxide and diphenyl sulfide may be caused by steric hindrance.

The crux of the matter is that the distance between N and N' in 4'-nitro-4-amino-substituted diphenyl oxide and diphenyl sulfide (8 – 8.5 A) is comparable with the distance between the end groups of the acylating agent – 4-nitrobenzoyl chloride (7.5 – 7.8 A), so that the introduction into the 4' position of a polar group (NO_2) considerably reduces the probability that a reaction will take place with substances containing similarly oriented polar groups (NO_2, COCl). These hindrances are absent in the case of biphenyl derivatives. The observed fall in reaction rate of disubstituted diphenyl oxides and diphenyl sulfides in comparison with monosubstituted derivatives is evidently due to a considerable extent to steric factors rather than to the conditions of transmission of the reciprocal influence of the substituents.

Most of the physicochemical data (ultraviolet absorption spectra, dipole moments, etc.) indicate that transmission of the reciprocal influence of substituents through sulfur atoms is hindered in aromatic compounds. This statement is supported by structural investigations on diphenyl sulfide derivatives. According to x-ray analyses [4] the 4,4'-dibromodiphenyl sulfide molecule is not planar, the benzene rings being at an angle towards one another, and the angle formed with the plane of the sulfur and bromine atoms is approximately 40°. Such a molecular configuration does not facilitate transmission of the reciprocal influence of substituents from one ring to the other.

Since the material in the cited papers indicates that work will continue in the field of application of chemical methods to the solution of the problem of transmission of reciprocal effects across heteroatoms, it seemed to us necessary to make our observations.

A solution of the problem in question calls for more extensive use of physical methods of investigation and a comprehensive study of the behavior of similar molecules.

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.

BASIC AND ACIDIC OXIDES OF METALS OF THE LARGE PERIODS OF THE PERIODIC SYSTEM[*]

S. A. Shchukarev

A useful approach to the problem of thermodynamic characterization of the basic and acidic functions of oxides is the comparison of the energy relations of pleiads of halides, especially chlorides, of a given element with the energetics of pleiads of the corresponding oxides. Such a comparison may provide data for an answer to the question: which oxides are bound to be basic (susceptible to neutralization by hydrochloric acid with formation of chlorides that are not hydrolyzable by water) and which, conversely, are not susceptible to neutralization, i. e., are acidic so that the chlorides are acid chlorides and easily hydrolyzed?

The energetic characterization is of course not the only useful approach, and an important light on the problem of basicity and acidity of oxides is thrown by the theory of transition from compounds with an ionic bond to compounds with a covalent bond; useful information is also provided by reactions of oxides with water. Nevertheless, thermodynamic relations can play a big part, if only because of the abundance of experimental data.

As a concrete example, we shall examine the behavior of vanadium, which gives, in the higher valence stages, V_2O_5, VF_5, VCl_4, VBr_3 and VI_3.

In Fig. 1 oxidation stages are plotted on the abscissas and the enthalpies of formation on the axis of the ordinates.

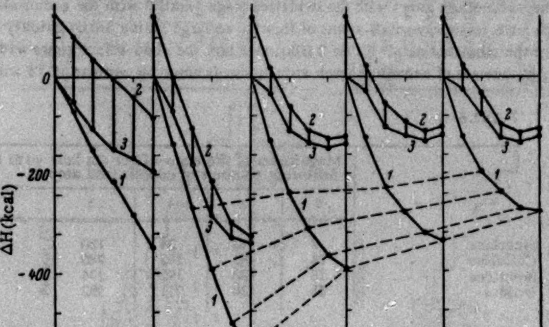

Fig. 1. Dependence of energy of formation of oxides, fluorides, chlorides, bromides and iodides of vanadium on the stages of oxidation (calculated per g-atom of metal). 1) Formation of gaseous compounds from free atoms; 2) formation of gaseous compounds from simple substances; 3) formation of solid compounds from elements. The differences between the ordinates of points of lines 2 and 3 are equal to the enthalpies of condensation.

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[*] Preceding communication, see [1].

We see from Fig. 1 that the energy of condensation of vanadium halides is lower than that of the oxides at the second stage; in addition it is seen that curves 1 for vanadium halides have a special characteristic which is hardly perceptible in the case of the oxides; this characteristic is reflected in the definite tendency of successive branches of the curves to be shortened with increasing oxidation stage; this tendency is particularly conspicuous in the case of the large atoms of iodine which appear to hinder one another in their efforts to approach closely to the central atom; such large atoms are therefore compelled in the case of atomic bonds (at high oxidation stages) to make use of more remote and less favorable (possibly even less perturbed) electronic orbits (4d, 4p, 4f instead of 3d), while in the case of ionic bonds (at low oxidation stages) they are compelled to utilize the lower portion of the Coulomb energy of the electrostatic field.

Although we do not claim absolute accuracy for the values listed in Table 1 (data used for vanadium halides [2]), we shall nevertheless attempt to evaluate the order of magnitude of the endo-effect of coordination, i. e., of that reduction in the molecular energy of gaseous molecules that depends on what we might describe as the repulsive influence of atoms arranged coordinatively round a given central atom. For the purpose of rough calculation of this magnitude we take as a measure of the endo-effect of coordination the deviation from additivity which would be expected in the simplest, idealized case if all the subsequent atoms of halogen (after the first) released as much energy as the first atom on combination with the central atom.

TABLE 1

	$\frac{1}{2}$ V_2O_5	VF_5	VCl_5	VBr_5	VI_5	TiO_2	TiF_4	$TiCl_4$	$TiBr_4$	TiI_4
Additive value (kcal)	365	670	630	630	610	320	640	520	496	440
True value (kcal)	352	550	390	336	278	318	541	411	372	308
Endo-effect of coordination	13	120	240	294	332	2	99	109	124	132

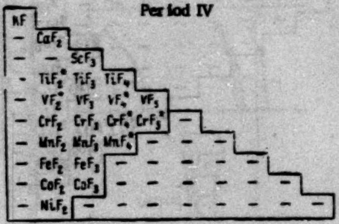
Due to the endo-effect of coordination, the curves 1 in Fig. 1 decrease in steepness with increasing stage of oxidation, i. e., the endo-effect grows with the oxidation stage parallel with the accumulation of coordinated atoms. The transition from relatively small atoms of fluorine to large iodine atoms quickly increases the endo-effect as evident from the tabulated data. Table 2 illustrates how the endo-effect grows with increasing number of coordinated atoms in the case of vanadium (such an increase is noted on comparing Ti with V).

TABLE 2

	Magnitudes of the endo-effect (in kcal with the following numbers of coordinated atoms			
	2	3	4	5
Fluorides	2	10	34	120
Chlorides	24	83	162	240
Bromides	28	120	192	294
Iodides	48	126	211	332

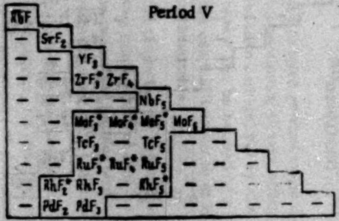
The low magnitude of the endo-effect in oxygen coordination is due partly to the size of the O atom being similar to that of the fluorine atom, as well as, of course, to the ability of the oxygen atom to replace two atoms of fluorine.

Unfortunately, too little is known with certainty about the heats of formation of halides of metals of groups V and VI; moreover, even the data for the thermochemistry of chlorides of molybdenum and tungsten are of doubtful accuracy; no experimental thermochemical characterization of the halides of niobium and tantalum has previously been reported; the thermochemistry of halides of elements of group VIII has also been



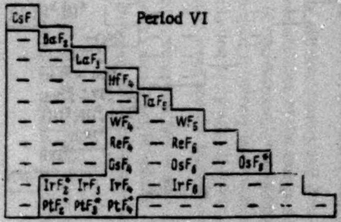
Period IV

KF									
—	CaF_2								
—	—	ScF_3							
-	TiF_2^*	TiF_3	TiF_4						
—	VF_2^*	VF_3	VF_4^*	VF_5					
—	CrF_2	CrF_3	CrF_4^*	CrF_5^*	—				
—	MnF_2	MnF_3	MnF_4^*	—	—	—			
—	FeF_2	FeF_3	—	—	—	—	—		
—	CoF_2	CoF_3	—	—	—	—	—	—	
—	NiF_2	—	—	—	—	—	—	—	—



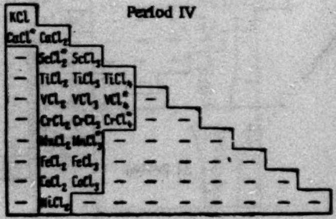
Period V

RbF									
—	SrF_2								
—	—	YF_3							
—	—	ZrF_3^*	ZrF_4						
—	—	—	—	NbF_5					
—	—	MoF_3^*	MoF_4^*	MoF_5^*	MoF_6				
—	—	TcF_3	—	TcF_5	—	—			
—	—	RuF_3^*	RuF_4^*	RuF_5	—	—	—		
—	RhF_2^*	RhF_3	—	RhF_5^*	—	—	—	—	
—	PdF_2	PdF_3	—	—	—	—	—	—	—



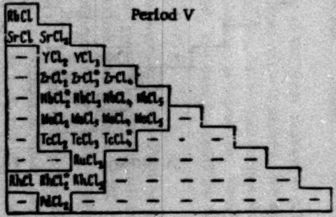
Period VI

CsF									
—	BaF_2								
—	—	LaF_3							
—	—	—	HfF_4						
—	—	—	—	TaF_5					
—	—	—	WF_4	—	WF_5				
—	—	—	ReF_4	—	ReF_6	—			
—	—	—	OsF_4	—	OsF_6	—	OsF_8^*		
—	IrF_2^*	IrF_3	IrF_4	—	IrF_6	—	—	—	
—	PtF_2^*	PtF_3^*	PtF_4^*	—	—	—	—	—	—



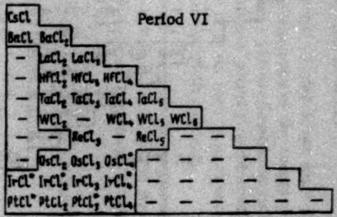
Period IV

KCl									
CaCl*	$CaCl_2$								
—	$ScCl_2^*$	$ScCl_3$							
—	$TiCl_2$	$TiCl_3$	$TiCl_4$						
—	VCl_2	VCl_3	VCl_4^*	—					
—	$CrCl_2$	$CrCl_3$	$CrCl_4^*$	—	—				
—	$MnCl_2$	$MnCl_3^*$	—	—	—	—			
—	$FeCl_2$	$FeCl_3$	—	—	—	—	—		
—	$CoCl_2$	$CoCl_3$	—	—	—	—	—	—	
—	$NiCl_2$	—	—	—	—	—	—	—	—



Period V

RbCl									
SrCl	$SrCl_2$								
—	YCl_2	YCl_3							
—	$ZrCl_2^*$	$ZrCl_3^*$	$ZrCl_4$						
—	$NbCl_2^*$	$NbCl_3$	$NbCl_4$	$NbCl_5$					
—	$MoCl_2$	$MoCl_3$	$MoCl_4$	$MoCl_5$	—				
—	$TcCl_2$	$TcCl_3$	$TcCl_4^*$	—	—	—			
—	—	$RuCl_3$	—	—	—	—	—		
RhCl	$RhCl_2^*$	$RhCl_3$	—	—	—	—	—	—	
—	$PdCl_2$	—	—	—	—	—	—	—	—



Period VI

CsCl									
BaCl	$BaCl_2$								
—	$LaCl_2$	$LaCl_3$							
—	$HfCl_2^*$	$HfCl_3$	$HfCl_4$						
—	$TaCl_2$	$TaCl_3$	$TaCl_4$	$TaCl_5$					
—	WCl_2	—	WCl_4	WCl_5	WCl_6				
—	—	$ReCl_3$	—	$ReCl_5$	—	—			
—	$OsCl_2$	$OsCl_3$	$OsCl_4^*$	—	—	—	—		
IrCl*	$IrCl_2^*$	$IrCl_3$	$IrCl_4^*$	—	—	—	—	—	
PtCl*	$PtCl_2$	$PtCl_3^*$	$PtCl_4$	—	—	—	—	—	—

Period IV

KBr									
—	$CaBr_2$								
—	$ScBr_2^*$	$ScBr_3$							
—	$TiBr_2$	$TiBr_3^*$	$TiBr_4$						
—	VBr_2	VBr_3	VBr_4^*	—					
—	$CrBr_2$	$CrBr_3$	—	—	—				
—	$MnBr_2$	—	—	—	—	—			
—	$FeBr_2$	$FeBr_3^*$	—	—	—	—	—		
—	$CoBr_2$	—	—	—	—	—	—	—	
—	$NiBr_2$	—	—	—	—	—	—	—	—

Period V

$RbBr$									
—	$SrBr_2$								
—	YBr_2	YBr_3							
—	$ZrBr_2^*$	$ZrBr_3^*$	$ZrBr_4$						
—	$NbBr_2$	$NbBr_3$	—	$NbBr_5$					
—	$MoBr_2$	$MoBr_3$	$MoBr_4^*$	—	—				
—	—	$TcBr_3$	—	—	—	—			
—	—	$RuBr_3$	—	—	—	—	—		
$RhBr^*$	$RhBr_2^*$	$RhBr_3$	—	—	—	—	—	—	
—	$PdBr_2$	—	—	—	—	—	—	—	—

Period VI

$CsBr$									
—	$BaBr_2$								
—	$LaBr_2$	$LaBr_3$							
—	$HfBr_2$	$HfBr_3^*$	$HfBr_4$						
—	$TaBr_2$	$TaBr_3$	—	$TaBr_5$					
—	WBr_2	—	WBr_4^*	WBr_5	WBr_6^*				
—	—	$ReBr_3^*$	—	—	—	—			
—	$OsBr_2^*$	$OsBr_3^*$	$OsBr_4$	—	—	—	—		
$IrBr$	$IrBr_2$	$IrBr_3$	—	—	—	—	—	—	
$PtBr^*$	$PtBr_2$	$PtBr_3$	$PtBr_4$	—	—	—	—	—	—

Period IV

KI									
—	CaI_2								
—	—	ScI_3							
—	TiI_2	TiI_3^*	TiI_4						
—	VI_2	—	—	—					
—	CrI_2	CrI_3	—	—	—				
—	MI_2	—	—	—	—	—			
—	FeI_2	FeI_3^*	—	—	—	—	—		
—	CoI_2	—	—	—	—	—	—	—	
—	MI_2	—	—	—	—	—	—	—	—

Period V

RbI									
—	SrI_2								
—	—	YI_3							
—	ZrI_2^*	ZrI_3^*	ZrI_4						
—	NbI_2	NbI_3	-	NbI_5					
—	MoI_2	-	MoI_4^*	—	—				
—	—	TcI_3	—	—	—	—			
—	—	RuI_3	—	—	—	—	—		
RhI^*	RhI_2^*	RhI_3	—	—	—	—	—	—	
—	PdI_2	—	—	—	—	—	—	—	—

Period VI

CsI									
—	BaI_2								
—	—	LaI_3							
—	HfI_2	HfI_3^*	HfI_4						
—	TaI_2^*	TaI_3^*	-	TaI_5					
—	WI_2	-	WI_4^*	—	—				
—	—	ReI_3^*	—	—	—	—			
—	—	—	OsI_4	—	—	—	—		
IrI	IrI_2	IrI_3	—	—	—	—	—	—	
PtI	PtI_2	PtI_3	PtI_4	—	—	—	—	—	—

inadequately studied. In order, therefore, to characterize the role of the endo-effect of coordination, we shall limit ourselves here to listing the hitherto known fluorides, chlorides, bromides and iodides of metals of the even series of the system. The starred items are unstable compounds; the blank spaces correspond to compounds not existing in practice in the free, condensed state and in macroscopic quantities.

These diagrams are self-explanatory and show convincingly that the shift of the upper limit actually depends not only on the over-all slope of the energy curves and the magnitudes of the energy of condensation but also on the endo-effect of coordination. The latter effect increases: 1) from fluorides to iodides; 2) from elements of period VI (with their relatively large atoms) to the elements of period IV (with central atoms of smaller size and increased perturbation energies); 3) from Ca to Ni, from Sr to Pd, from Ba to Pt, once again due to the reduced sizes of the central atom and the increased perturbation energy of its electrons.

Going back to Fig. 1, we cannot fail to note the great difference between the diagrams for the oxides and fluorides of vanadium, which shows that in spite of the proximity of fluorine to oxygen in the system there is a considerable difference between the thermodynamic characteristics of their compounds with the same element (vanadium).

We note the following data on moving along the horizontal row of the system and comparing the nitride, oxide and fluoride of vanadium at the same oxidation stage (the third):

	VN	$^1/_2V_2O_3$	VF_3
$\Delta H_{stand.}$(kcal)	—41	—145	—285

It is clear that there is some general cause not only leading to the great increase in $\Delta H_{stand.}$ on passing from fluoride to oxide, but continuing to take effect on transition from oxide to nitride. We do not yet possess quantitative data for vanadium carbide, but by analogy with other carbides we can assume that the transition from nitride to carbide would also be marked by a large fall in enthalpy of formation. Numerous facts certainly support the theory that the cause of interest to us is generally valid; the data for vanadium may be typical of a whole class of analogous phenomena.

In view of the great interest of an explanation of the above-discussed observations for chemistry (in particular due to the numerous implications of such an explanation) we propose to consider this problem more closely, with special reference to oxides and halides of the alkali and alkaline earth metals. In this case the argument is very considerably simplified since these oxides and halides can be regarded as ionic compounds.

It was clear at the start that the main obstacle to the formation of ionic oxides (and more so of nitrides) is the considerable energy necessary for charging atoms of oxygen and nitrogen with two and three electrons, respectively. The orders of magnitude of this energy are: for O^{-2} +168 kcal; for N^{-3} approximately +700 kcal.

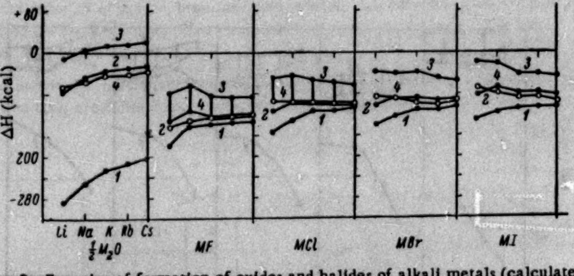


Fig. 2. Energies of formation of oxides and halides of alkali metals (calculated for 1 g-atom of metal). 1) Formation of gaseous molecules from free ions; 2) formation of gaseous molecules from neutral atoms; 3) formation of gaseous molecules from solids; 4) formation of solids from elements.

Due to the high endo-effects of the charge, the over-all exo-balance of the energy of formation of the compounds is sharply reduced, and in the case of nitrides and (especially) carbides the sign may be changed to give an endo-balance. Conversely, the electron affinity of univalent halogen atoms is negative, i. e., the over-all balance $\Delta H_{\text{stand.}}$ increases in the case of halides. Data for the energetics of compounds of the alkali metals are plotted in Fig. 2, which shows that the simplest relations exist between curves 1. Curve 1 for the oxides is approximately 1.5 times lower than curve 1 of fluorides, which was to be expected from electrostatic considerations; curves 1 for the fluorides, chlorides, bromides and iodides are arranged one above the other, and this arrangement also has a simple explanation; all of the curves 1 are identical in character, i. e., they rise from the lithium point to the cesium point, as is entirely natural.

TABLE 3

	Energy of transition of electrons from atoms of metals into oxygen or halogen (in kcal)					Note
	Li	Na	K	Rb	Cs	
O	211	202	184	180	174	$I + E_{1/2\,O^{=}}$
F	44	35	17	13	7	$I - E_{G^{-}}$
Cl	40	31	13	7	4	
Br	44	35	17	13	7	
I	55	46	28	24	18	

The most interest is attached to the transition from curves 1 to curves 2, the vertical distances between whose points are equal to the sum of the energies of ionization of the metal and the energy of charging of neutral atoms of O, F, Cl, Br and I.

Since singly-charged halogen ions are formed by exothermic reaction, in practice the addition (allowing for the signs of the effects) of the endo-effect of ionization of the atom of alkali metal to the exo-effect of the charging of the halogen atom results in the case of halides in a small endo-effect; the charging of $^1/_2\,O^{=}$ requires an endo-effect of 84 kcal; together with the endo-effect of the ionization of the atoms of alkali metal, this gives a still higher endo-value (see Table 3).

In the case, therefore, of oxides, curve 2 is very much higher than curve 1, and the rises are small for halides.

Due to the high energies of ionization of atoms of Li and Na, the form of curve 2 in the case of halides differs appreciably from that of curves 1.

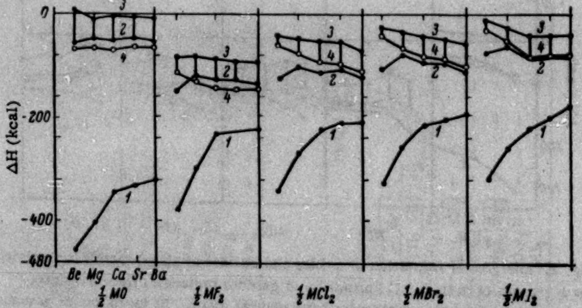


Fig. 3. Energies of formation of oxides and halides of alkaline earth metals (calculated for 1 g-equiv. of metal). 1-3) Formation of gaseous compounds from ions; 4) formation of solids from elements.

Transitions from curves 2 and 3 and subsequently to 4 shift the curves of oxides and halides upwards and then downwards to an equal extent; due to the high energies of sublimation of sodium and, in particular, lithium, and due also to the specific features of the energies of the crystal structures, the curves are again slightly distorted and acquire the standard form familiar to all chemists. We may note that the energies of condensation of oxides of the alkali metals do not greatly differ in order of magnitude from the energies of condensation of halides (especially fluorides).

A different picture is presented by Fig. 3 in which curves 1-4 for compounds of the alkaline earth metals are plotted.

Curves 1, as in Fig. 2, are simple and understandable; the only difference is that the points of the oxides lie not 50% lower than the points of the fluorides but approximately 33%, which is consistent with electrostatic requirements.

The transitions from curves 1 to curves 2 now have a different appearance, since they correspond not to $I_I - E_{G^-}$ or $I_1 + E_{1/2O^=}$, but to $^1/_2 (I_I + I_{II}) - E_{G^-}$ or $^1/E (I_I + I_{II}) + E_{1/2O^=}$; since the half-sum of the first and second ionization potentials is considerably larger than I_I, the rises from curves 1 to curves 2 are here larger than in the case of compounds of the alkali metals, and they are larger not only for oxides but also for halides (Table 4).

TABLE 4

	Energy of transition of electrons from atoms of metals to O or halogen (kcal)					Notes
	Be	Mg	Ca	Sr	Ba	
Oxides	401	345	291	276	259	$^1/_2 I_I + {}^1/_2 I_{II} + E_{1/_2 O^=}$
Fluorides	233	178	124	109	92	$^1/_2 I_I + {}^1/_2 I_{II} - E_{G^-}$
Chlorides	230	175	121	106	89	
Bromides	233	178	124	109	92	
Iodides	244	189	135	120	103	

Just as in the case of alkali metals, curve 2 for oxides is at a lower level than curves 2 for halides. The transition from 2 to 3 follows the same course as with the alkali metals, but the transition from 3 to 4 (i. e., allowing for the energies of condensation) appreciably changes the picture. Whereas the energies of condensation of halides of the alkali metals only differ insignificantly from the energy of condensation of their oxides, in the case of the alkaline earth metals only the fluorides (but with the exception of BeF_2) have energies of condensation not far from the magnitude of the energies of condensation of the oxides. The energies of condensation rapidly fall off in the order of chlorides, bromides, and iodides; this behavior probably reflects the commencing tendency to pass from purely ionic crystalline structures to molecular structures. The largest fall is noted for Be; it is slightly less for Mg (Table 5).

Owing to the relatively small magnitudes of the energies of condensation, substances like $BeCl_2$, $BeBr_2$, $MgBr_2$, BeI_2, MgI_2 and CaI_2 are formed less exothermically than the corresponding oxides. A comparison of the

TABLE 5

	Energy of condensation in kcal/1 g-equiv [2]									
	Li	Na	K	Rb	Cs	Be	Mg	Ca	Sr	Ba
O	60	55	55	60	60	79	60	69	64	52
F	63	72	52	48	48	30	50	60	55	50
Cl	48	55	51	51	45	17	30	45	46	40
Br	45	49	48	50	46	15	30	40	41	40
I	46	49	44	45	44	14	21	28	35	38

data for $\Delta H_{stand.}$ is plotted in Fig. 4, which contains curves of $\Delta H_{stand.}$ of oxides and halides of elements of groups I and II as well as data for compounds of elements of groups III and IV. We see here a continuation of the process of gradual penetration of the oxides curve into the region of the halide curves, which commences in groups I and II. It is true that in groups III and IV we can no longer make such simple and clear-cut calculations as in the case of the nearly purely ionic compounds of groups I and II, but the experimental values nevertheless reveal a further development of the process of gradual increase of the competing ability of the oxides in relation to the halides; this process is bound up more or less with the higher energies of condensation of the oxides, with the increased volatility of the halides, and with the development of an appreciable endo-effect of coordination which rapidly increases for the halides with increasing number of the group. These aspects are illustrated by Figs. 5 and 6, plotted for compounds of elements of groups III and IV in a similar manner to Figs. 2 and 3.

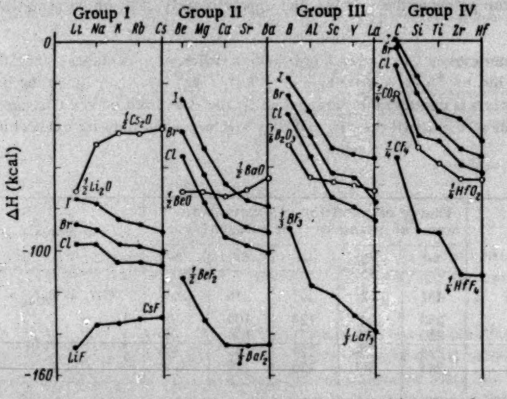


Fig. 4. Standard energies of formation of oxides and halides of elements of groups I to IV of the periodic system (calculated per 1 g-equiv.).

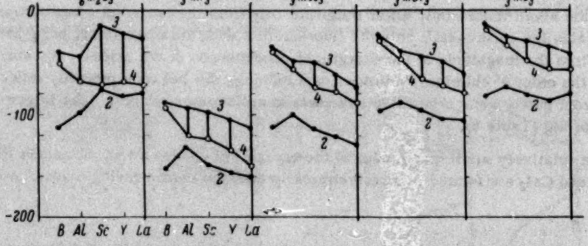


Fig. 5. Energies of formation of oxides and halides of elements of group III (calculated per g-equiv.). 2,3) Formation of gaseous compounds from atoms and elements; 4) the same for standard values.

One of our objectives was to show (as illustrated by Figs. 5 and 6) what an important and even decisive part is played by the enthalpy of condensation of gases and in turn by the properties and structure of the crystals in the chemical characterization of such important classes of compounds as halides and oxides.

In illustration of what has just been said, we again proceed to compare oxides and halides (more specifically chlorides in order to simplify the picture), and we depict the competition of chlorine and oxygen within the framework of the periodic law in the form of graphs corresponding to successive periods of the system (Fig. 7).

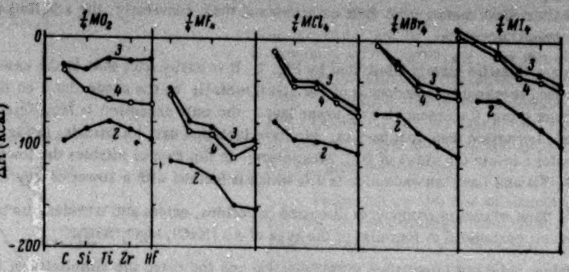


Fig. 6. Energies of formation of oxides and halides of elements of group IV (calculated per g-equiv.). 2,3) Formation of gaseous compounds from atoms and elements; 4) the same for standard values.

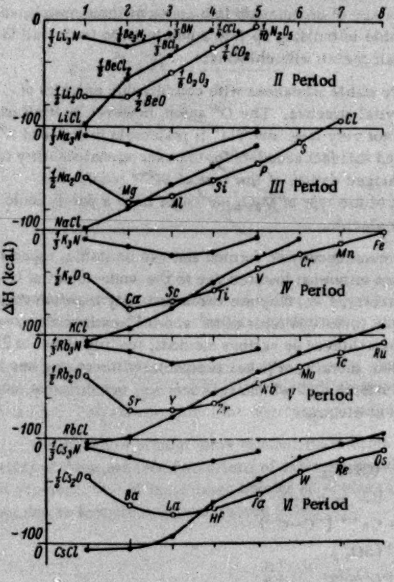


Fig. 7. Standard energies of formation of oxides, chlorides and nitrates (per g-equiv.) for elements of periods II to VI of the periodic system.

We see that in the second period of the system only the point of $^1/_2 Li_2O$ lies appreciably higher than the LiCl point, and therefore lithium oxide must be basic in character and must easily change into the salt LiCl on neutralization. Gaseous HCl acts on $^1/_2 Li_2O$ in such a manner that $^1/_2$ mole of water vapor is formed in place of HCl, and this process is accompanied by a supplementary exo-effect of 7 kcal; it is also easy to calculate the thermal effect in presence of liquid water, when it is necessary to allow for the heat of solution, the energy of condensation of water vapor and the energy of hydration of the oxides.

We already find an opposite picture in the case of beryllium: the energy of formation of a g-equivalent of beryllium oxide exceeds the energy characterizing beryllium chloride; this excess is small, and beryllium oxide is amphoteric and easily hydrolyzed.

Oxides of boron and carbon are weakly acidic: their points lie below the points of the chlorides.

Thus, the most characteristic property of oxides (their basicity or acidity) is revealed by the form, the mutual position and the intersection of the curves of the oxides and chlorides, and this intersection depends in large measure on the energy of condensation of oxides and chlorides. The same intersection also reveals hydrolytic reactions — as the converse of neutralization processes.

In period III the positions of the points of the oxides of Na and Mg endow them with a basic character, while aluminum is seen to be amphoteric, and Si, P, S and Cl are acidic.

The basic properties of Na are more strongly developed than those of Li because the distance between the Na_2O and NaCl points is greater than the distance between the Li_2O and LiCl points. In period IV, apart from K and Ca, Sc also acquires a basic character, as clearly shown in Fig. 7.

In periods V and VI the picture is similar to the diagram for period IV.

In his "Principles of Chemistry" D. L. Mendeleev [3] specially noted that the alkali metals are capable of displacing the alkaline earth metals from their chlorides and that, conversely, the alkaline earth metals displace the alkali metals from their oxides.

These facts are likewise clearly illustrated by Fig. 7. It is easily seen that in the case of chlorides the maximum energy is indeed released by compounds of the alkali metals; on the oxide lines, on the other hand, the point of the oxides of group II elements is at a lower level; the only exception is lanthanum, which releases more energy during oxide formation than does barium. We have included data for nitrides in Fig. 7 in order to further develop and to better explain the views of D. I. Mendeleev; in the case of nitrides the lowest points are in group III – for AlN, ScN, YN and LaN; an exception is BN, which is formed with a lower energy than beryllium nitride.

In all of the three classes of compounds discussed (chlorides, oxides and nitrides) the minimum points on the energy curves thus correspond to formulas of the type of AB (NaCl, MgO, AlN).

D. I. Mendeleev attached importance to this relation and indicated the simplicity of the formula in the course of an attempt at explanation.

We now see that this truly noteworthy circumstance, which confirms to some extent Dalton's hypothesis of the existence of a principle of maximum simplicity for the formulas of the most probable chemical compounds, is based on the energy concept. The absence of an endo-effect of coordination for molecules MX, the low energy of ionization of atoms of the alkali metals, the negligible energy of dissociation into atoms of these metals, and the quite high energy of condensation of molecules MX capable of building up into a purely ionic lattice all help to account for the exceptional stability of compounds of alkali metals with chlorine.

In the case of oxides we are dealing with exceptionally stable substances with considerable energies of condensation, and for this it is desirable to have an ionic crystal structure. The $O^{=}$ anion, however, is itself unstable since it is formed endothermically, and M^{+} cation of not very large size (Li^{+} is preferable to Na^{+} and K^{+}) are suitable for its stabilization; better still are M^{++} ions, and this fact accounts for the exceptional stability of the oxides of the alkaline earth metals. Still more highly charged cations of the type of M^{+++} require too much energy for their formation, especially since molecules of the type of M_2O_3 no longer have a purely ionic structure and release less energy per g-equiv than the MO molecule.

Although ionic oxides of the type of M_2O and MO can consequently be formed and can be stable, especially in the solid state, their energies of formation are nevertheless somewhat lowered due to the endo-effect of $O^{=}$ formation, and for this reason these oxides have a basic character, i. e., they are exothermically transformed into chlorides and in general behave as if they had remained in the inviolable form of M^{+} and M^{++} cations after having got rid of the energetically unfavorable $O^{=}$ anion; this can be achieved by various methods, leading either to disappearance of the free negative charges or to reduction in their number, or (what is especially interesting and important) to their dissipation, scattering or spread (i. e., to distribution of two charges over any two different atoms). Such are, for example, the following processes of dissipation of electrons.

$$Ca^{++}O^{=} + H_2O = Ca^{++}(OH^{-})_2$$

$$Ca^{++}O^{=} + 2HCl = Ca^{++}(Cl^{-})_2 + H_2O$$

$$Ca^{++}O^{=} + 3C = CO + Ca^{++}({}^{-}C{-}C^{-})$$

$$Ca^{++}O^{=} + SO_3 = Ca^{++}(SO_4^{=})$$

$$Ca^{++}O^{=} + CO_2 = Ca^{++}(CO_3^{=})$$

In the last three examples doubly-charged anions are formed whose negative charges are spread, since they are not attached to the same atom. Multi-charged and at the same polyatomic anions are also encountered extremely rarely in the free state (in a gaseous discharge), which affords evidence of their poor stability or even of their complete instability; at the same their existence is more probable than that of monoatomic ions of $O^{=}$, $N^{=}$, etc. Stabilization of polyatomic anions in crystals and in solutions evidently proceeds with very much greater facility than the stabilization of monoatomic ions.

Characteristic of the simplest nitrides of an ionic nature is the presence of the $N^{\equiv}$ anion, which is even more unstable than the $O^{=}$ anion. Due to the very large endo-effect of formation of $N^{\equiv}$, its stabilization is

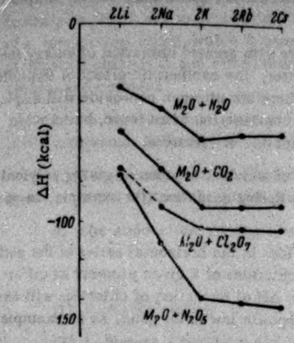


Fig. 8. Energy of combination of oxides of the alkali metals with water and acidic oxides.

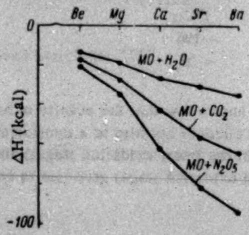


Fig. 9. Energies of combination of oxides of the alkaline earth metals with water and acid anhydrides.

better effected with the help of the relatively small cations of Li^+ and Be^{++}, but even more suitable are the cations of Al^{+++}, Sc^{+++}, etc. For this reason the most stable nitrides are actually found in group III of the system. In addition, due to the presence of the unstable $N^{\equiv}$, nitrides are still less exothermic than oxides, and ΔH curves of their formation fall in Fig. 7 into a region not far from the zero line.

Following out this line of reasoning, it is easy to see that the ionic carbides must lie at a still higher level and must enter the endo-region. In order to avoid the energetically very unfavorable $C^{≣}$ ions, the compound is transformed into atomic (nonionic), crystalline structures of the diamond type (case of SiC) or proceeds to lose its negative charges by dissipation with formation of diatomic anions, of the type of $^-C\equiv C^-$ for example, and gives rise to the acetylides of lithium and calcium which still appear in the exo-region but higher than the nitrides.

In the foregoing discussion we referred to the principle of dissipation of negative charges, i. e., to the tendency of these charges not to remain at one atom only. It is well known, of course, that multi-charged cations are likewise formed with difficulty, but in chemistry we have many examples, nevertheless, of fully stable, doubly-charged and at the same time monoatomic cations; we also encounter triply-charged cations and even occasionally quadruply-charged ones. There is a dissymmetry in the ratio of anions to cations: the multiply-charged anions that we know to be stabilized by the energy of crystallization and solvation are predominantly only monoatomic, i. e., with charges shared between different atoms, for example, $SO_4^{=}$, $CO_3^{=}$, etc.; $O^{=}$, $S^{=}$ and $N^{\equiv}$ ions are developed in exceptional cases by especially firm stabilization by their partners and always strive to disappear by transformation into other substances. Polyatomic anions are therefore encountered in compounds more frequently than polyatomic cations.

We shall now present some characteristic cases of dissipation reactions of negative charges. The most important of these are transformations of oxides of the alkali and alkaline earth metals into peroxides, superoxides and ozonides. All of these cases involve an exothermic reaction which is accompanied by dissipation of the electrons due to formation of coordinated bonds.

$$\begin{matrix}K^{+}\\K^{+}\end{matrix}O^{=} + {}^{1}/_{2}O_2 = \begin{matrix}K^{+}\\K^{+}\end{matrix}(O^{-}—O^{-})$$

$$\begin{matrix}K^{+}\\K^{-}\end{matrix}O^{=} + {}^{3}/_{2}O_2 = K^{+}(^{-}O—O) + K^{+}(O^{-}—O)$$

Compounds such as BeO and Li_2O are the least readily transformed into peroxides since the $O^{=}$ ions are stabilized in them by small cations.

A similar case was discovered in our laboratory by S. M. Arria [4] who succeeded in synthesizing barium pernitride, i. e., in realizing the dissipation of the charges of the nitrogen anion; this compound has the formula BaN_2 or Ba^{++} ($^-N=N^-$) and is an analog of BaO_2 in a certain sense.

Still more interesting as examples of electron dissipation processes are reactions in which hydrates of basic oxides and salts are formed, i. e., the process of combination of two oxides. The exothermic effects of such processes, in which the energetically unfavorable $O^=$ anions disappear, are plotted in Figs. 8 and 9 for the simplest compounds of the alkali and alkaline earth metals.

We see that in these cases the carbonates are formed from the oxides with greater liberation of energy than the basic hydrates of the oxides, and therefore CO_2 will neutralize the latter; the exothermic effect of formation of nitrates is even greater than that of the formation of carbonates, and therefore nitrogen pentoxide will displace CO_2 from carbonates. But it is still more characteristic that processes of combination of an ionic, basic oxide with water and acid anhydrides are exothermic and accompanied by dissipation of electrons.

Analogous examples could also be adduced for sulfides, the $S^=$ ion of which is capable of giving polyions with added atoms of sulfur, or hydrosulfide anions and polyatomic anions during oxidation (for example, on passing from Na_2S to Na_2SO_4) or on combination of basic sulfides with acids.

We have compared the ΔH of formation of higher oxides and chlorides in the horizontal series of the periodic system. We obtain a similar picture if we compare the oxides and chlorides of a given element at different oxidation stages. In this case again, at the lower oxidation stages the ΔH of formation of chlorides will exceed the ΔH of formation of the oxides, while at the higher stages the opposite law holds good. As an example, we present data for titanium compounds.

	TiO	$^1/_2\ Ti_2O_3$	TiO_2
ΔH (kcal)	—122	—181.5	—225.6
	$TiCl_2$	$TiCl_3$	$TiCl_4$
ΔH (kcal)	—124	—172	—196
Δ	—2	~10	~30

From the foregoing considerations we arrive logically at the well-known law that the acidity or basicity of an oxide is governed not only by the chemical nature of the oxidized element but also to a considerable extent by the degree of oxidation. Both manganese (a typical cationogen in the lower oxidation stages) and chlorine (an element characterized by a great electron affinity in the seventh oxidation stage) give rise to typical acidic oxides.

SUMMARY

1. An oxide may be characterized as a base by the amount by which the enthalpy of formation of the chloride of the same metal exceeds the enthalpy of formation of the oxide (at the same oxidation stage).

When the enthalpy of formation of an oxide considerably exceeds the enthalpy of formation of the corresponding chloride, the latter is susceptible to hydrolysis and can be characterized as an acid chloride, while the oxide itself will be acidic. When the enthalpies of formation of chloride and oxide are very similar, the oxide is amphoteric.

2. In the case of a metal capable of forming a series of oxides, the curves of $\Delta H_{\text{stand.}}$ versus oxidation stage (calculated on 1 g-atom of metal) are so arranged that the curve of the chlorides is at the lower oxidation stages below the curve of the basic oxides; after intersection of the curves (at the amphoteric oxide) the curve of the chlorides for high oxidation stages moves above the curve of the oxides. This law can be utilized for evaluation of the enthalpy of formation of oxides and chlorides for which few data are available.

3. On plotting the curves of enthalpies of formation (calculated per g-atom of oxidized element) of higher oxides and chlorides of elements in the same series of the periodic system, we observe intersection of the curves. Due to this intersection, the oxides TiO_2, V_2O_5, CrO_3 and Mn_2O_7 are acidic; the acidity of Mn_2O_7 is accordingly associated with the ability of Mn to give an oxide at a high (seventh) oxidation stage.

4. The relative position of the curves which has just been mentioned is not solely associated with the energies of the interatomic bonds; it also depends: a) on the endo-effect of formation of $O^=$ ions, which decreases the enthalpy of formation of basic (lower) oxides; b) on the endo-effect of coordination of the atoms of chlorine round the central atom which lowers the enthalpy of formation of the higher chlorides; c) on the fall in the exo-effect of the energy of condensation of gaseous compounds in the case of chlorides with increasing stage of oxidation which is very much faster than in the case of oxides.

5. Neutralization of basic oxides by acid anhydrides (CO_2,N_2O_5) depends on the tendency of the electrons to dissipate, i. e., not to accumulate at one atom ($O^=$, $N^≡$, etc.) but to spread themselves over different atoms of a monatomic anion, which is energetically favorable. The same cause (the unprofitableness of accumulation of negative charges at one atom) results in the enthalpy of formation falling in the order of chlorides, oxides, nitrides and carbides.

6. An explanation is given of D. I. Mendeleev's observation of the tendency of elements to form particularly stable compounds in formation of substances with the formula AB.

7. It was noted that the endo-effect of coordination increases: a) from fluorides to iodides; b) from elements of period VI to elements of period IV; c) from Ca to Ni, from Sr to Pd and from Ba to Pt.

8. The endo-effect of coordination of oxygen atoms is considerably lower than for fluorine atoms.

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Received March 12, 1957

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* Original Russian pagination. See C. B. translation.

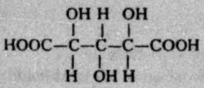
THE DISSOCIATION CONSTANTS OF TRIHYDROXYGLUTARIC ACID

N. K. Davidenko

Hydroxycarboxylic acids and their compounds with metals have recently attracted an increasing amount of attention due to the importance which they are acquiring in science and technology. At the same time very little work has been done on the physicochemical properties of these acids, and any work at all in this field has been concentrated on a small number of hydroxyacids. Tartaric acid is the member of the hydroxydicarboxylic acid series that has attracted most attention. Trihydroxyglutaric acid differs from tartaric acid in containing one more $\text{H}-\overset{|}{\underset{|}{\text{C}}}-\text{OH}$ group. Its physicochemical properties have scarcely been studied. A number of investigations have indicated, however, the possibility of obtaining cheap trihydroxyglutaric acid and of employing it in place of tartaric and citric acids.

The purpose of the present work is to determine the first and second acid dissociation constants of optically active xylotrihydroxyglutaric acid* (A) with the help of potentiometric titration.

The first acid dissociation constant of xylotrihydroxyglutaric acid was calculated by Ruff [1] on the basis of the electrical conductivity of its solutions. At 25° it was found equal to $6.6 \cdot 10^{-4}$. There are no data for the second acid dissociation constant in the literature.



$$\text{HOOC}-\overset{\text{OH}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{OH}}{\text{C}}}-\overset{\text{OH}}{\underset{\text{H}}{\text{C}}}-\text{COOH}$$

(A)

Materials. For the preparation of solutions we started from previously purified commerical trihydroxyglutaric acid,made at the pilot plant of the Fergana wood hydrolysis works,which before purification contained 99% of trihydroxyglutaric acid.** To the hot, concentrated solution of this trihydroxyglutaric acid was added active carbon for decoloration of the solution) and pulverized BaS in small portions until the filtered solution no longer gave a reaction for the $SO_4^=$ ion. The solution was filtered, concentrated on a water bath and rapidly cooled. The acid separated in finely crystalline form and was isolated from the mother liquor and recrystallized from aqueous solution. The acid was washed on the filter with a little water and then with ethyl alcohol, and was dried at first in the air and then in a desiccator over sulfuric acid. The so purified trihydroxyglutaric acid had m. p. 134°.

Solutions of trihydroxyglutaric acid were made up by weight. The NaOH solution used for titration was free of CO_2 and was prepared by the procedure of Kolthoff and Sandell [2].

Apparatus. The "Orion" pH-meter (type 2512 with a glass electrode) was used for measurements of pH. The comparison electrode was a saturated calomel electrode.

The temperatures of the solutions were kept constant to within 0.1° in a thermostat.

Results of potentiometric titration of a 0.005 M solution of trihydroxyglutaric acid with alkali at 20° are plotted in the diagram. In the measurements 40 ml of acid of the above concentration was titrated with 0.1045 N NaOH solution. In the diagram the pH value is plotted against the number of equivalents of alkali added per mole of acid present in the original solution.

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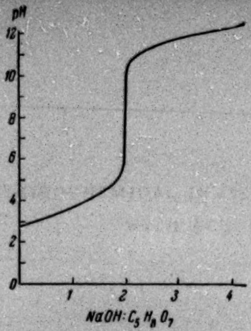
[*] In the further course of this paper xylotrihydroxyglutaric acid will be called simply trihydroxyglutaric acid.

[**] We obtained this acid from the All-Union Institute of Research of the Hydrolysis and Sulfite Cellulose Industry.



Titration of trihydroxyglutaric acid.

The titration curve does not exhibit a potential jump corresponding to the neutralization of the first hydrogen ion. The inflection on the titration curve corresponds to the addition of two equivalents of alkali per mole of acid. This testifies to the closeness between the values of the first and second dissociation constants.

The pH of the neutral solution, found from the titration curve, is 7.8. The titration curve does not indicate the removal of hydrogens from the alcohol groups on further addition of alkali to a pH of ~ 12.

Due to the close similarity between the values of K_1 and K_2, the calculation of K_1 from the formula $pH = = {}^1/2\ pK_1 + {}^1/_2 \log C_K$ may be seriously in error. Calculation of K_2 from the pH of the acid salt may also include a serious error due both to the entry of K_1 into the formula and to the similarity between K_2 and C_K [3]. We therefore made use of the system of equations based on the law of mass action for calculation of the constants of acid dissociation of trihydroxyglutaric acid.

Different mathematical variants are known of this method which is used for calculation of the dissociation constants of polybasic acids and of the instability constants of their compounds with metals [3-6]. We made use of the algebraic variant of the method described by Martell and Calvin [6] when they calculated the dissociation constants of ethylenediamine tetraacetic acid.

We use the following symbols: $\underline{a}$ is the number of equivalents of alkali used up in the titration; $[TpH_2]$ is the concentration of undissociated trihydroxyglutaric acid, $[TpH^-]$ is the concentration of anions of the monosubstituted sodium salt, $[Tp^{2-}]$ is the concentration of anions of the disubstituted sodium salt, $[H^+]$ is the hydrogen ion concentration, C_K is the total molar concentration of all of the forms of the acid (ionic and molecular).

The following equation will be valid for all of the points of the potentiometric titration curve with $\underline{a} < 2$:

$$[TpH_2] + [TpH^-] + [Tp^{2-}] = C_k \tag{1}$$

It follows from the requirement of electrical neutrality of the solution that:

$$aC_k + [H^+] = [TpH^-] + [Tp^{2-}], \tag{2}$$

since the concentration of $[Na^+]$ ions = aC_K.

Results of Calculation of the Dissociation Constants of Trihydroxyglutaric Acid at 20° ($C_K = 5 \cdot 10^{-3}$)

No. of point	a	pH	$[H^+]$	$K_1 \cdot 10^4$	$K_2 \cdot 10^5$
1	0.3135 1.2540	3.02 4.01	$9.56 \cdot 10^{-4}$ $9.78 \cdot 10^{-8}$	8.3	6.8
2	0.5225 1.1495	3.21 3.87	$6.16 \cdot 10^{-4}$ $1.35 \cdot 10^{-4}$	8.1	6.1
3	0.4180 1.0450	3.11 3.76	$7.77 \cdot 10^{-4}$ $1.74 \cdot 10^{-4}$	8.3	5.8
4	0.2090 0.9405	2.93 3.65	$1.17 \cdot 10^{-3}$ $2.24 \cdot 10^{-4}$	8.3	5.0
5	0.6270 1.4630	3.29 4.30	$5.13 \cdot 10^{-4}$ $5.01 \cdot 10^{-5}$	8.8	6.9
	Mean value		. . . . .	8.4	6.1

From the equation of the first dissociation stage:

$$TpH_2 \rightleftarrows H^+ + TpH^-$$

we have:

$$K_1 = \frac{[H^+][TpH^-]}{[TpH_2]} \qquad (3)$$

From the equation of the second dissociation stage:

$$TpH^- \rightleftarrows Tp^{2-} + H^+$$

we have:

$$K_2 = \frac{[H^+][Tp^{2-}]}{[TpH^-]} \qquad (4)$$

On solving the system of four equations (1)-(4) for K_1 and K_2 and eliminating the unknowns $[TpH_2]$, $[TpH^-]$ and $[Tp^{2-}]$, we obtain:

$$K_2\left\{\frac{(2-a)\,C_x}{[H^+]}-1\right\}-\frac{1}{K_1}[H^+]\,(aC_x+[H^+])=(a-1)\,C_x+[H^+] \qquad (5)$$

On inserting the values of $[H^+]$ calculated from potentiometric titration data when $a < 2$, we obtain a series of pairs of equations with two unknowns, K_1 and K_2. By solving these equations we obtain the values of both of the constants.

The table contains the results of calculations for five pairs of points. The calculations were actually carried out for a larger number of points of the titration curve; the deviations of the results from the mean lie within the same limits as those presented in the table.

SUMMARY

The dissociation constants of xylotrihydroxyglutaric acid at 20° were calculated from potentiometric titration data. The values obtained were $K_1 = 8.4 \cdot 10^{-4}$; $K_2 = 6.1 \cdot 10^{-5}$.

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Received February 13, 1957

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PHYSICOCHEMICAL INVESTIGATION OF THE INTERACTION OF ACETONE WITH ACETIC ACID AND ITS DERIVATIVES

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Previous papers [1-4] described investigations of the reaction of urea with acetic acid and its derivatives. It was established that chemical reaction in the system is intensified with increasing substitution of chlorine for the hydrogen atoms in the acetic acid radical. A similar trend was observed in systems of acetamide with acetic acid and its chloro-derivatives [5-8]. It was found that replacement of one amino group in urea by a methyl group leads to still greater intensification of chemical interaction, which is reflected to a large extent in the composition-property diagrams and in the isotherms of electrical conductivity, viscosity, surface tension and density.

TABLE 1

Density (d) and Viscosity (η) in the System Acetone–Acetic Acid

CH_3COOH mole%	0°		20°		30°	
	d	η	d	η	d	η
0	—	—	0.806	0.44	0.791	0.39
10	0.849	0.57	0.835	0.50	0.819	0.44
20	0.874	0.66	0.858	0.56	0.845	0.49
30.2	0.900	0.77	0.883	0.62	0.870	0.53
39.8	0.921	0.87	0.905	0.69	0.896	0.60
50.1	0.950	1.01	0.930	0.79	0.918	0.67
60.3	0.973	1.17	0.954	0.89	0.949	0.75
69.8	0.997	1.33	0.981	0.99	0.972	0.84
80.0	1.022	1.50	1.006	1.10	0.999	0.90
89.8	1.047	1.63	1.033	1.19	1.025	0.96
94.9	1.060	1.69	—	—	—	—
100	1.075	1.73	1.057	1.25	1.053	1.053

TABLE 2

Surface Tension in the System Acetone–Acetic Acid

CH_3COOH mole%	0°	20°	30°
0	—	24.43	23.29
10	27.34	25.12	24.15
20	27.88	25.74	24.84
30	28.33	26.32	25.45
40	28.70	26.85	26.05
50	29.05	27.25	26.45
60	29.35	27.52	26.73
70	29.60	27.72	26.85
80	29.75	27.87	27.00
90	29.75	27.85	27.00
100	29.70	27.74	26.90

TABLE 3

Density (d), Viscosity (η) and Surface Tension (σ) in the System Acetone–Monochloroacetic Acid

$CH_2ClCOOH$ mole%	20°			30°			40°		
	d	η	σ	d	η	σ	d	η	σ
0	0.806	0.44	24.43	0.791	0.39	23.29	0.786	0.35	21.95
10	0.864	0.55	25.84	0.860	0.48	24.83	0.853	0.48	23.60
20	0.935	0.70	27.55	0.924	0.61	26.64	0.917	0.52	25.31
30	0.999	0.92	29.35	0.982	0.77	28.45	0.975	0.65	26.90
40	1.060	1.21	31.40	1.053	0.99	30.40	1.042	0.83	28.80
50	1.126	1.68	33.31	1.117	1.33	32.13	1.105	1.05	30.64
60	1.184	2.16	35.32	1.180	1.76	34.05	1.166	1.38	32.35
70	—	—	—	—	—	—	1.234	1.85	34.07

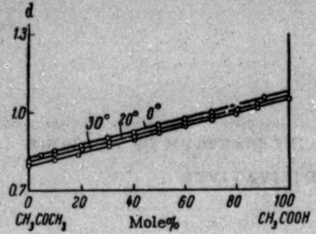

Fig. 1. Density in the system acetone—acetic acid.

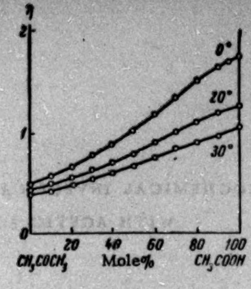

Fig. 2. Viscosity in the system acetone—acetic acid.

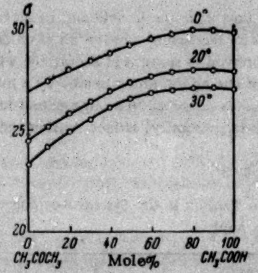

Fig. 3. Surface tension in the system acetone—acetic acid.

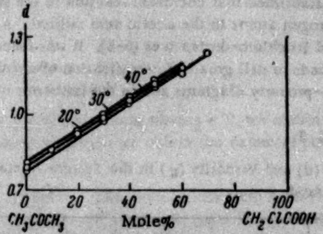

Fig. 4. Density in the system acetone—monochloroacetic acid.

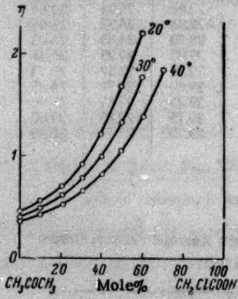

Fig. 5. Viscosity in the system acetone—monochloroacetic acid.

It appeared of interest to study the character of the interaction of acetone with acetic acid and its chloroderivatives in order to check the validity of the theoretical assumptions made previously [6] about the nature of the chemical bond in systems consisting of urea and acetamide on the one hand and acetic acid and its chloroderivatives on the other, and involving the presence of a hydrogen bond.

In the present paper we present the results of investigation of three binary systems: acetone—acetic acid, acetone—monochloroacetic acid, and acetone—trichloroacetic acid.* The viscosity, density and surface tension were studied. We described the experimental procedure previously [2, 5, 9].

Concentrations were expressed in molar percentages, viscosities in centipoises, and surface tensions in dynes/cm. The starting substances were purified: acetone by three redistillations, acetic acid by freezing, trichloroacetic acid by distillation.

The literature does not contain any data for the fusibility of the systems acetone—acetic acid (or its chloroderivatives). In our laboratory we likewise failed to obtain fusibility data.

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* E. G. Veselkova participated in the experimental work.

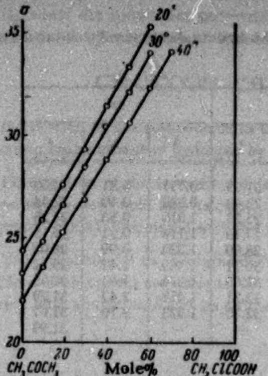

Fig. 6. Surface tension in the system acetone—monochloroacetic acid.

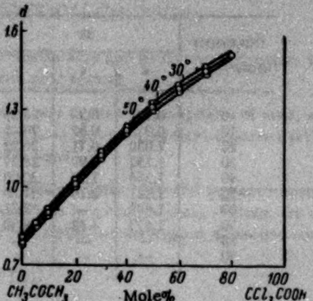

Fig. 7. Density in the system acetone—trichloroacetic acid.

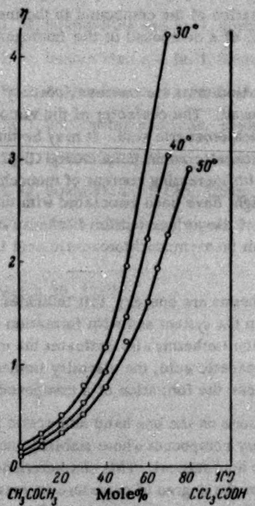

Fig. 8. Viscosity in the system acetone—trichloroacetic acid.

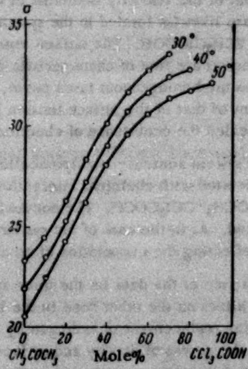

Fig. 9. Surface tension in the system acetone—trichloroacetic acid.

We studied the system acetone—acetic acid in the liquid phase on the basis of data for density, viscosity and surface tension at 0, 20 and 30° (Figs. 1-3; Tables 1 and 2).

The system acetone—monochloroacetic acid was studied in the liquid phase on the basis of data for density, viscosity and surface tension at 20, 30 and 40° (Figs. 4-6; Table 3).

In the case of the system acetone—trichloroacetic acid, the density, viscosity and surface tension were studied at 30, 40 and 50° (Figs. 7-9; Table 4).

TABLE 4

Density (d), Viscosity (η) and Surface Tension (σ) in the System Acetone−Trichloroacetic Acid

CCl_3COOH (mole%)	30°			40°			50°		
	d	η	σ	d	η	σ	d	η	σ
0	0.791	0.39	23.29	0.786	0.35	21.95	0.771	0.31	20.60
10	0.915	0.52	24.45	0.899	0.45	23.43	0.889	0.40	22.44
20	1.030	0.71	26.22	1.017	0.61	25.27	1.010	0.53	24.25
30	1.137	0.99	28.27	1.125	0.83	27.18	1.118	0.71	26.15
40	1.234	1.37	30.00	1.225	1.12	28.90	1.220	0.99	28.00
50	1.331	2.16	31.60	1.320	1.67	30.71	1.309	1.42	29.52
60	1.408	—	32.71	1.393	2.43	31.65	1.374	1.81	30.55
70	1.477	4.42	33.50	1.465	3.23	32.31	1.453	2.47	31.29
80	—	—	—	—	—	32.70	1.523	3.10	31.67
90	—	—	—	—	—	—	—	—	31.99

DISCUSSION OF RESULTS

The viscosity isotherms of the system acetone−acetic acid are S-shaped. This points to the existence of a compound in the fused homogeneous medium with the composition $2CH_3COOH \cdot CH_3COCH_3$. The decreasing steepness of the curve with rising temperature is due to the dissociation of the compound in the melt. The convexity of the surface tension isotherm is also a sign of the presence of a compound in the homogeneous medium. The maximum bulge corresponds to a 2 : 1 compound.

In the system acetone−monochloroacetic acid the viscosity isotherms are concave, possibly due to dissociation of an associated component and the formation of a compound. The character of the viscosity isotherms resembles that of the viscosity isotherms in the system urea−monochloroacetic acid. It may be thought that two compounds are likewise formed in the system acetone−monochloroacetic acid: $CH_3COCH_3 \cdot CH_2ClCOOH$ and $CH_3COCH_3 \cdot 2CH_2ClCOOH$. The surface tension alters smoothly with increasing content of monochloroacetic acid, and the isotherms are free of characteristic discontinuities that might have been associated with the formation of compounds in the homogeneous fused phase. However, the shape of the surface tension isotherms of this system is reminiscent of that of the surface tension isotherms of the system urea−monochloroacetic acid in which other methods revealed the occurrence of chemical interaction.

In the system acetone−trichloroacetic acid the density isotherms are convex; this indicates a slight contraction associated with chemical interaction of the components in the system and with formation of the compound $CH_3COCH_3 \cdot CCl_3COOH$. The convexity of the surface tension isotherms also indicates the existence of a 1 : 1 compound. As in the case of the system acetone−monochloroacetic acid, the viscosity isotherms are concave, thus reflecting the dissociation of an associated component and the formation of a compound.

Comparison of the data for the three systems shows that acetone on the one hand and acetic acid and its chloro-derivatives on the other hand in the liquid phase form binary compounds whose stability increases slightly with increasing replacement of hydrogen by chlorine in the acetic acid radical. This characteristic is particularly reflected on the curves of density and surface tension. In the latter the degree of curvature increases on passing from the system acetone−acetic acid to the system acetone−trichloroacetic acid. It should be noted that of the three components − urea, acetamide and acetone − acetamide reacts more vigorously than the others with acetic acid and its chloro-derivatives, due to its higher dielectric constant (acetamide has a constant of 59.10, and acetone one of 21.45). Therefore when organic acids dissolve in acetamide, the degree of dissociation with cleavage of a hydrogen ion is greater. This facilitates the formation of more stable compounds of acetamide with acetic acid and its chloro-derivatives [10].

SUMMARY

1. The systems acetone−acetic acid, acetone−monochloroacetic acid and acetone−trichloroacetic acid were investigated by the methods of measurement of density, viscosity and surface tension.

2. In a homogeneous fused medium, the system acetone–acetic acid contains the compound $2CH_3COOH \cdot CH_3COCH_3$, while the system acetone–trichloroacetic acid contains the compound $CCl_3COOH \cdot CH_3COCH_3$. It is suggested that the system acetone–monochloroacetic acid contains the compounds

$$CH_2ClCOOH \cdot CH_3COCH_3 \text{ and } 2CH_2ClCOOH \cdot CH_3COCH_3.$$

3. Interaction of the components in the systems acetone–acetic acid and its chloro-derivatives increases with increasing replacement of hydrogen by chlorine in the acetic acid radical.

4. Examination of the isotherms of density, viscosity and surface tension in the systems of urea, acetamide and acetone with acetic acid and its derivatives leads to the conclusion that the chemical processes taking place in these systems are all associated with the presence of a hydrogen bond.

5. The stabilities of the compounds formed in the systems urea–, acetamide– and acetone–acetic acid (and its chloro-derivatives) are compared. The most stable compounds in a homogeneous medium are compounds of acetamide with acetic acid and its chloro-derivatives, since acetamide has the highest dielectric constant.

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Received March 26, 1957

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INVESTIGATION OF THE INTERACTION OF DIPHENYLAMINE WITH ORGANIC ACIDS BY THE METHODS OF PHYSICOCHEMICAL ANALYSIS

N. K. Tsvetkova and D. E. Dionis'ev*

Aromatic amines are more weakly basic than aliphatic amines, since the electronegative benzene ring lowers the basicity of an aromatic amine. Especially strongly depressed are the basic properties of secondary, purely aromatic amines such as diphenylamine which contains two benzene rings. It was therefore of interest to study the nature of the interaction of diphenylamine with substances possessing acidic properties, i. e., organic acids.

Equimolar compounds are formed by diphenylamine with hydrochloric, hydrobromic and sulfuric acids: $C_{12}H_{11}N \cdot HCl$, $C_{12}H_{11}N \cdot HBr$, $C_{12}H_{11}N \cdot H_2SO_4$. With hydrofluoric acid it gives two compounds: $C_{12}H_{11}N \cdot 2HF$ and $C_{12}H_{11}N \cdot 3HF$. With nitric acid the compounds $4C_{12}H_{11}N \cdot HNO_3$ and $3C_{12}H_{11}N \cdot 2HNO_3$ were isolated.

The following compounds of diphenylamine with aliphatic acids are known: a compound of diphenylamine with lauric acid $C_{12}H_{11}N \cdot C_{11}H_{23}COOH$ detected by O. A. Osipov and N. A. Trifonov [1] by the methods of physicochemical analysis; a compound of diphenylamine with oxalic acid $C_{12}H_{11}N \cdot C_2H_2O_4$ [2] and a stable, thermally undissociatable compound of diphenylamine with maleic acid $C_{12}H_{11}N \cdot C_4H_2O_3$, obtained by O. A. Osipov and Iu. V. Fedorov [3].

EXPERIMENTAL

Experimental procedure. Diphenylamine was recrystallized 3 times from ligroine and dried in a desiccator in a stream of warm air. The purified product had m. p. 53°. Monochloroacetic acid was purified by distillation and had m. p. 63° and b. p. 186.5°. Trichloroacetic acid (chemically pure grade) was redistilled 3 times and kept in sealed ampoules; m. p. 59° and b. p. 197°. p-Nitrobenzoic acid (chemically pure grade) was purified by numerous recrystallizations and had m. p. 238°. Salicylic acid (chemically pure grade) was also purified by numerous recrystallizations and had m. p. 159.8°. Succinic acid (chemically pure grade) was recrystallized and then had m. p. 184.5°. Adipic acid (chemically pure) had m. p. 151°.

The visual-polythermal method was employed for investigation of the fusion behavior and for determination of the melting points of the pure substances. We established the temperatures of appearance of the first crystals by cooling down of the fused mixture, and we determined the temperatures of disappearance of the last crystals on melting. The agreement between the two temperatures indicated that equilibrium had been attained from both directions [4].

The substance was placed in a test tube provided with a thermometer and stirrer. More uniform heating and cooling was effected by putting the test tube in a glass housing.

Densities were measured with the Reno pycnometer with a narrow neck and a capacity of 4.5 ml. Viscosities were determined in an Ostwald viscometer of the open type.

Electrical conductivity was measured by the Kohlrausch method in a closed cell using a smooth platinum electrode. The current source was a lamp generator of sonic frequency with an amplifier. For the purpose of improving the accuracy of measurement, the minimum of the current was stepped up with a two-lamp amplifier and then picked up on the recorder (high-ohmic telephones and "magic eye").

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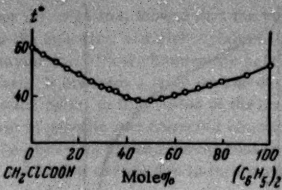

Fig. 1. Fusibility curve of the system diphenylamine–monochloroacetic acid.

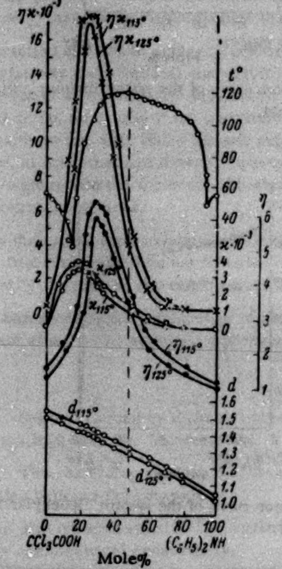

Fig. 2. Curve of fusion, viscosity (η), density (d), specific electrical conductivity (κ) and corrected electrical conductivity (κ · η) of the system diphenylamine–trichloroacetic acid.

Densities, viscosities and electrical conductivities were measured in a glycerol thermostat which enabled the temperature to be kept constant to within 0.1°.

Mixtures were made up by individual weighings. Concentrations were calculated in molar percentages; viscosities were expressed in centipoises.

Examination of binary systems of diphenylamine with organic acids. The system diphenylamine–monochloroacetic acid had not previously been studied. We investigated it by the fusion method (Fig. 1). The fusion curve consists of two branches – diphenylamine and monochloroacetic acid – which intersect at the eutectic point corresponding to 50 mole% and 37.5°.

System diphenylamine–trichloroacetic acid. This was here examined for the first time, using data for fusion, viscosity, density and specific electrical conductivity (Fig. 2). The fusion curve has a maximum corresponding to 50 mole% of diphenylamine, indicating the formation in the solid phase of a compound of equimolar composition which melted considerably higher than the pure components. Whereas the melting point of the highest melting component (trichloroacetic acid) is 59°, the compound melts at 112.5°. The fusion curve has two eutectics – at 50.5° and 97 mole%, and at 25° and 15 mole% of diphenylamine. The specific electrical conductivity, viscosity and density of the system were examined at 115 and 125°. The viscosity isotherms contain a maximum corresponding to 30 mole% of diphenylamine in the mixture. The density isotherms are slightly concave to the axis of concentrations.

The specific electrical conductivity isotherms contain a maximum corresponding to 25 mole% of diphenylamine in the mixture; the maximum is considerably higher than that of the component with the highest conductivity. Correction of the electrical conductivity for viscosity κ · η does not eliminate the maximum but merely shifts it slightly in the direction of diphenylamine. In the opinion of some investigators [4] the chemical compound in the system is characterized by a minimum of electrical conductivity. A whole series of systems of this type was investigated, however, and in these the reaction is reflected by a maximum of electrical conductivity that does not disappear when the viscosity correction is applied [5-7]. According to M. I. Usanovich [8], the persistence of the maximum on the curve of corrected electrical conductivity testifies to the occurrence of acid–base interaction in the system. In the present case, however, the position of the maximum is no guide as to the composition of the compound formed in the liquid phase.

System diphenylamine–p-nitrobenzoic acid. We studied this system on the basis of fusion data (Fig. 3). The two branches of the curve intersect at a eutectic corresponding to a 98 mole% of diphenylamine.

System diphenylamine–salicylic acid. We also studied this system only by fusion observations (Fig. 4). The fusion curve comprises a long branch of diphenylamine. The eutectic point is considerably shifted onto the side of diphenylamine and corresponds to 97 mole% of the latter.

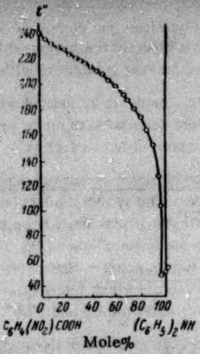

Fig. 3. Fusion curve of the system diphenylamine-p-nitrobenzoic acid.

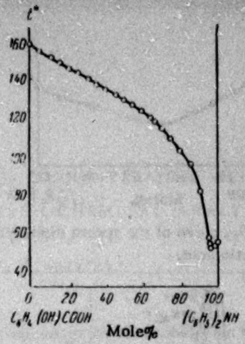

Fig. 4. Fusion curve of the system diphenylamine-salicylic acid.

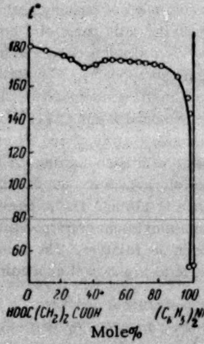

Fig. 5. Fusion curve of the system diphenylamine-succinic acid.

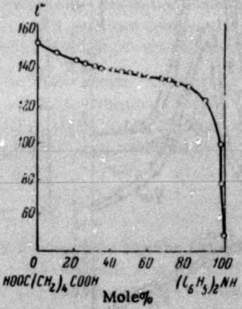

Fig. 6. Fusion curve of the system diphenylamine-adipic acid.

System diphenylamine–succinic acid. The fusion curve (Fig. 5) contains a maximum corresponding to the compound $C_{12}H_{11}N \cdot C_4H_6O_4$ with m. p. 177.5°, and two eutectic points – at 172° and 33.4 mole%, and 52° and 99.5 mole% of diphenylamine.

System diphenylamine–adipic acid. A slight fall in melting point is observed on the portion of the fusion diagram (Fig. 6) from 0 to 90 mole%, which indicates closeness to the limiting mutual solubility of the components. Fusion curves of similar form were obtained by F. V. Alekseev [9] when studying the system salicylic acid–water and by O. A. Osipov [10] for the system butyric acid–picric acid.

DISCUSSION OF RESULTS

It follows from the results obtained that systems formed by organic acids with diphenylamine do not exhibit chemical interaction in the overwhelming majority of cases.

In a study of the interaction of diphenylamine with acetic acid, N. A. Trifonov [11] established the absence of formation of any chemical compound between the components. Introduction of the electronegative chlorine atom into the acetic acid molecule facilitates cleavage of a hydrogen ion, i. e., it intensifies the acidity of the compound. Hence in substances of basic character we should expect intensification of interaction in the order:

$$CH_3COOH \rightarrow CH_2ClCOOH \rightarrow CHCl_2COOH \rightarrow CCl_3COOH.$$

Our investigations showed that the introduction of one chlorine atom into the acetic acid molecule does not alter the behavior, and diphenylamine does not react with monochloroacetic acid. Study of the interaction of diphenylamine with trichloroacetic acid revealed the existence of the compound $C_{12}H_{11}N \cdot CCl_3COOH$ in the solid phase; it occupies a large portion of the phase diagram of the system. The viscosity curves possess a maximum, which points to interaction of the components also in the liquid phase. This is confirmed by the form of the curves of specific and corrected electrical conductivity which also exhibit maxima. The position of the maxima on the above-mentioned curves does not correspond to the composition of a compound. The density curves are convex, indicating contraction in the system.

Lengthening of the chain of the acid molecule usually leads to weakening of the acidic properties of a compound. Propionic and butyric acids accordingly do not react with diphenylamine [12]. On the other hand, lauric acid [2], with a very much smaller dissociation constant than that of butyric acid (10^{-12} and $1.48 \cdot 10^{-5}$, respectively) reacts with diphenylamine to form an equimolar compound.

Reaction of benzoic acid with diphenylamine was studied by A. Baskov [13] who made observations on fusion, viscosity and electrical conductivity. None of his data reflected interaction between the components. Introduction of electronegative substituents into benzoic acid intensifies the mobility of the hydrogen of the carboxyl group, especially if the substituent is in the ortho-position. Thus, salicylic acid gives molecular compounds with amines with which benzoic acid does not interact, for example, with α- and β-naphthylamines [14]. However, as our researches showed, diphenylamine does not react with salicylic acid. Nor does the introduction of a nitro group into the molecule of benzoic acid alter the behavior. Diphenylamine does not form compounds with p-nitrobenzoic acid.

In the system diphenylamine–succinic acid the fusion method revealed the formation of an equimolar compound. Diphenylamine does not react with adipic acid; a tendency to form layers is observed in this system, as reflected by the form of the fusion curve.

Consequently, the introduction of another benzene ring into the aniline molecule has a remarkably strong depressant effect on its activity; diphenylamine is less reactive than aniline.

SUMMARY

1. Systems formed by diphenylamine with monochloroacetic, salicylic, p-nitrobenzoic, succinic and adipic acids were studied by the fusion method.

2. The phase diagrams of all of these systems, except with succinic acid, indicate absence of chemical interaction between the components.

3. The system formed by diphenylamine with trichloroacetic was studied by observations on fusion, density, viscosity and electrical conductivity.

4. It was established that the presence of two benzene rings in the diphenylamine molecule greatly lowers its susceptibility to complex formation.

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Received March 27, 1957

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PHYSICOCHEMICAL ANALYSIS OF THE SYSTEM ETHYLENEDIAMINE – ALLYL MUSTARD OIL

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Systems formed by mustard oils with secondary amines are typical rational systems [1]. In an investigation of the viscosity of systems of this class, N. S. Kurnakov and S. F. Zhemchuzhnyi showed [2] that they undergo reaction according to the equation

$$\mathrm{S{=}C{=}NR + NHR^{1}_{2} = CS(NHR)(NR^{1}_{2})},$$

with formation of substituted thioureas; the latter are transparent substances that do not break down under normal conditions. Curves of all of the physical properties of such systems possess a singular point whose position corresponds to the composition of the compound.

At the present time systems that have been closely examined are those comprising on the one hand allyl mustard oil and on the other hand aniline, piperdine, the isomeric toluidines; also systems of phenyl mustard oil with diethylamine, methyl- and ethylaniline, etc. [1-4].

In the present work we studied the interaction in the system allyl mustard oil–ethylenediamine by methods of physicochemical analysis.

For this purpose we made use of measurements of viscosity, density, refractive index, and boiling point; we also determined the composition of the vapor.

The components of the system were carefully purified. Allyl mustard oil was dried with freshly calcined calcium chloride and redistilled. We selected the cut boiling at 149.5-150.5° (752.7 mm). We isolated ethylenediamine from its hydrochloride, and dried it first with solid potassium hydroxide and then with metallic sodium before distilling it over the latter to obtain a product with b. p. 116.5-116.7° at 753.5 mm; $n^{20}D$ and $n^{18}D$ 1.5273 and 1.4578, respectively.

Considerable heat was released when the components were mixed, and caused the liquid to boil. In order to avoid losses, the substances were gradually mixed in Landolt vessels while being adequately cooled.

The viscosity was measured at 40° in two Ostwald viscometers of the closed type with capillaries of different diameters.

The viscometer with the larger diameter of capillary was used for the more viscous mixtures (50-80 mole% of mustard oil). This viscometer was calibrated with castor oil. Densities were measured in a pycnometer with a capacity of 1.2173 ml. The refractive index was determined at 35° in an Abbe refractometer. Results of measurements of these physical properties are presented in Table 1.

Boiling points and vapor compositions were determined in an apparatus of our own design operating on the principle of the ebullioscopic apparatus of V. A. Kireev [5]. The pressure in the apparatus was maintained to an accuracy of ± 0.3 mm Hg by a manostat with electromagnetic control. Boiling points of the system were determined at 100 and 200 mm Hg; vapor compositions were determined at 100 mm. Results are in Table 2.

The viscosity isotherm of the system (Fig. 1) consists of two branches, convex in relation to the axis of composition and intersecting in a sharp singular point at 66.7 mole% of mustard oil, thereby reflecting the presence

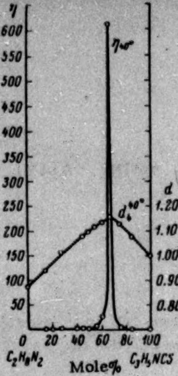

Fig. 1. Viscosity and density of the system ethylenediamine—allyl mustard oil.

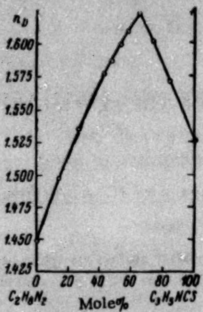

Fig. 2. Isotherm of the refraction index in the system ethylenediamine—allyl mustard oil.

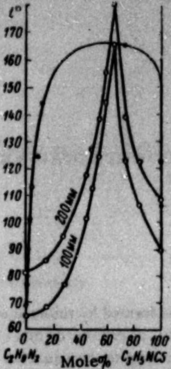

Fig. 3. Boiling points and vapor composition in the system ethylenediamine—allyl mustard oil.

TABLE 1

C_3H_5NCS in sol'n (mole%)	η^{40} (in poises)	d_4^{40}	n_D^{35}
0.00	0.007611	0.8713	1.4496
15.00	0.02956	0.9385	1.4974
27.94	0.06678	1.0120	1.5350
45.15	0.71457	1.0803	1.5775
49.48	1.55380	1.0963	1.5663
54.96	6.48500	1.1156	1.5994
59.94	24.7040	1.1333	1.6083
66.70	610.970	1.1548	1.6217
75.02	2.81410	1.1263	1.6010
85.10	0.55460	1.0740	1.5712
100.0	0.00592	0.9985	1.5252

TABLE 2

C_3H_5NCS (mole%)		Boiling point (pressures in mm Hg)	
in liquid phase	in vapor at 100 mm	100	200
0.00	0.0	65.0	81.3
15.00	0.2	68.6	85.8
27.94	1.1	76.7	94.8
45.15	3.1	101.5	117.6
49.48	4.6	113.1	127.3
54.96	9.8	124.5	138.7
59.94	13.6	144.7	155.7
66.70	74.7	165.6	179.5
75.02	100.0	123.1	139.0
85.10	100.0	106.7	122.5
100.0	100.0	89.8	108.5

in the system of the undissociated compound $C_2H_8N_2 \cdot 2C_3H_5NCS$. A striking feature is the enormous value of the viscosity of this substituted thiourea (η^{40} = 610.97 poises) or 80,275 times higher than the viscosity of ethylenediamine (the most viscous component). The prepared ethylenedi(allylthiourea) is considerably more viscous than the product of interaction in the system phenyl mustard oil—diethylamine [2], hitherto considered to be the most viscous of the substituted thioureas.

The high value of the viscosity of such compounds is usually associated not only with their strong supercooling but also with considerable association [4].

The isotherm of the density d^{40}_4 of the system comprises two nearly rectilinear branches (Fig. 1) intersecting at an acute angle to give a singular point corresponding to 66.7 mole% of oil and characterizing the formation of the above-noted substituted thiourea.

The isotherm of the refraction index $n^{35}D$ (Fig. 2) has a well-defined singular maximum corresponding to 66.7 mole% of oil, which agrees with the viscosity and density data in indicating the formation of an undissociated compound in the system.

Chemical interaction in the system is reflected in the results of the ebulliometric examination of the system. The boiling point curves (Fig. 3) for 100 and 200 mm Hg, plotted from the data of Table 2, each consist of two branches that intersect in a singular point whose position does not alter with changing pressure; it corresponds to the compound $C_2H_8N_2 \cdot 2C_3H_5NCS$. The condensation curve, obtained for 100 mm Hg, has a maximum that touches the liquid line at its singular point (Fig. 3). The singular point is weakly developed on the condensation curve although there is no doubt as to its existence.

A noteworthy feature is the form of the condensation curve. Its branches pass close to the ordinates of the components and then sharply inflect to come together at an acute angle. This may be due to the resulting compound having a high boiling point and a higher value for the heat of vaporization. Due to this, the vapor phase of the majority of the solutions, apart from those is close proximity to the compound, consists of nearly pure components.

In the light of the results obtained, the system ethylenediamine—allyl mustard oil must be regarded as a rational system. Inspection of the property curves shows that their singular points, including the point on the boiling isobar, correspond to the same composition – 66.7 mole% of allyl mustard oil. The azeotropic mixture in this system is probably, as in all rational systems, a true chemical compound. We have in this system a striking example of a singular boiling isobar whose course is consistent with the isotherms of viscosity and certain other properties.

SUMMARY

1. The system ethylenediamine—allyl mustard oil was investigated with the help of data for viscosity, density, refractive index and boiling point (at 100 and 200 mm Hg). The vapor composition over the solutions was also determined.

2. Only one compound is formed in the system – ethylene-di(allylthiourea), $C_2H_8N_2 \cdot 2C_3H_5CNS$. It is undissociated under normal conditions.

The system is an example of a rational system.

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Received February 25, 1957

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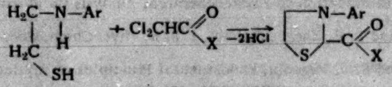
ETHYLENE SULFIDE IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS WITH TWO HETERO-ATOMS

VII. 3-ARYLTHIAZOLIDINE-2-CARBOXYLIC ACIDS AND THEIR DERIVATIVES

Iu. K. Iur'ev and S. V. Diatlovitskaia

The chemistry of thiazolidine and its derivatives has been studied most thoroughly and minutely in the case of thiazolidine-4-carboxylic acid, this being an important structural component of the penicillin molecule. As regards thiazolidine-2-carboxylic acid, neither the substance itself nor its derivatives has been reported up to now.

In one of our earlier works [1] we showed that N-(β-mercaptoethyl) arylamines readily enter into condensation with 1,1-dihaloalkanes, forming 3-arylthiazolidines. In the present work we carried out the same type of condensation with dichloroacetic acid, its amide, and its ester and obtained 3-arylthiazolidine-2-carboxylic acids, their amides, and their esters, respectively; from the latter we prepared the hydrazides.



(X = OH, NH_2, OC_2H_5, $NHNH_2$)

As also in the case of condensation of N-(β-mercaptoethyl) arylamines with methylene bromide [1], linear condensation products were obtained, together with 3-arylthiazolidine-2-carboxylic acids and their derivatives, in the condensations described in the present work. On distillation in vacuo they boiled over a wide range with appreciable decomposition and were not further investigated.

Study of the properties of 3-arylthiazolidine-2-carboxylic acids revealed that they decompose easily on treatment with acids. In connection with this, we could not prepare 3-o-tolyl- or 3-o-anisylthiazolidine-2-carboxylic acid either by the method given above or by hydrolysis of the esters of these acids with either 2 N hydrochloric or 50% acetic acid; when these esters were boiled with barium hydroxide solution, cleavage of the thiazolidine ring also occurred (appearance of a positive reaction for the sulfhydryl group).

The esters of 3-p-tolyl- and 3-p-anisylthiazolidine-2-carboxylic acids occur as colorless crystals. The esters of 3-phenyl-, 3-o-tolyl-, and 3-o-anisylthiazolidine-2-carboxylic acids are viscous oils which partially decompose on distillation in vacuo, owing to which it was impossible to obtain them in a perfectly pure state. Therefore, in order to characterize these esters, we prepared from them the corresponding 3-arylthiazolidine-2-carboxylic acid hydrazides.

Introduction of negatively charged groups ($-NH_2$, $-NH-NH_2$) into the carboxyl group led to the production of 3-arylthiazolidine-2-carboxylic acid derivatives which were somewhat more stable than the acids themselves; the amides and hydrazides of these acids do not decompose on strong heating, and they melt without decomposition (with the exception only of 3-phenyl- and 3-p-tolylthiazolidine-2-carboxylic acid amides); they are also quite stable to the action of acidic agents and decompose only on boiling with concentrated hydrochloric acid for 30-40 min.

EXPERIMENTAL

3-Arylthiazolidine-2-carboxylic Acids

3-Phenylthiazolidine-2-carboxylic acid. A mixture of 7.65 g (0.05 mole) of dichloroacetic acid, 7.5 g (0.09 mole) of anhydrous sodium acetate, 10.6 g (0.1 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 4 hrs in a water bath. The solid residue, obtained after driving off the alcohol, was put into a separatory funnel and shaken with a mixture of 1 N hydrochloric acid (100 ml) and ether (40 ml) until the residue was fully dissolved. After the ether layer was drawn off, the aqueous solution was extracted several more times with ether (a test sample of the aqueous solution had to remain clear on acidification with 2 N hydrochloric acid). The ether extract was dried with anhydrous magnesium sulfate.

After the ether was driven off, the residue crystallized. The crystals of 3-phenylthiazolidine-2-carboxylic acid were filtered out from the oil, washed with cold alcohol, and recrystallized from alcohol; m. p. 169-170° (decomp.). Yield, 5.2 g (50%).

Found %: C 57.13, 56.93; H 5.31, 5.40; N 6.55, 6.46; S 15.19, 15.38. M 209.0, 210.0. $C_{10}H_{11}O_2NS$. Calculated %: C 57.39; H 5.30; N 6.69; S 15.32; M 209.3.

3-p-Tolylthiazolidine-2-carboxylic acid. From 8.35 g of N-(β-mercaptoethyl)-p-toluidine and 7.75 g of dichloroacetic acid, 4.8 g (43%) of 3-p-tolylthiazolidine-2-carboxylic acid was obtained by the method given above; m. p. 164.5-165° (decomp.) (from alcohol).

Found %: C 59.59, 59.41; H 6.12, 6.22; N 6.11, 6.08. M 222.3, 223.2. $C_{11}H_{13}O_2NS$. Calculated %: C 59.16; H 5.87; N 6.27. M 223.3.

3-p-Anisylthiazolidine-2-carboxylic acid. A mixture of 9.15 g (0.05 mole) of N-(β-mercaptoethyl)-p-anisidine, 12.9 g (0.1 mole) of dichloroacetic acid, 7.5 g (0.09 mole) of anhydrous sodium acetate, 10.6 g (0.1 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 5 hrs in a water bath. To the oil, obtained after driving off the ether, was added 20 ml of 2 N hydrochloric acid, and the mixture was extracted with ether. (Part of the oily residue failed to dissolve in the ether and adhered to the walls of the flask and the separatory funnel in the form of tar.) The ether extract was dried with anhydrous magnesium sulfate.

The residue, obtained after driving off the ether, crystallized. The crystals of 3-p-anisylthiazolidine-2-carboxylic acid were filtered out from the oil, washed with cold alcohol, and recrystallized from alcohol; m. p. 130-130.5° (decomp.). Yield, 2.6 g (22%).

Found %: C 55.47, 55.50; H 5.60, 5.67; N 5.81. M 238.8, 240.0. $C_{11}H_{13}O_3NS$. Calculated %: C 55.21; H 5.48; N 5.85. M 239.3.

3-Arylthiazolidine-2-carboxylic acids are readily soluble in ether, acetone, and dichloroethane, poorly soluble in alcohol and benzene, and insoluble in water.

On heating with concentrated hydrochloric acid for 5-10 min 3-arylthiazolidine-2-carboxylic acids are cleaved; a positive reaction for the sulfhydryl group appears; on boiling with a concentrated solution of alkali the positive reaction for the sulfhydryl group appears after 1.5-2 hrs.

3-Arylthiazolidine-2-carboxylic Acid Amides

Procedure. A mixture of 0.05 mole of the N-(β-mercaptoethyl) arylamine, 0.075 mole (9.6 g) of dichloroacetamide, 0.06 mole (5 g) of anhydrous sodium acetate, 0.066 mole (7.5 g) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 4 hrs in a water bath. After distilling off the alcohol the solid residue was treated 5 times by shaking with a mixture of ether and water in a separatory funnel. The undissolved solid part – the 3-arylthiazolidine-2-carboxylic acid amide – was filtered out, washed with ether, and recrystallized from alcohol. The ethereal extract was dried with anhydrous magnesium sulfate. An additional small amount of amide crystals separated out from the oil obtained after driving off the ether.

TABLE 1

Amides	Yield in %	Melting point	C (%)		H (%)		N (%)	
			found	calc.	found	calc.	found	calc.
3-Phenylthiazolidine-2-carboxylic acid amide	30	171—172° (decomp.)	57.69, 57.43	57.66	5.96, 5.92	5.81	13.25, 13.21	13.45
3-p-Tolylthiazolidine-2-carboxylic acid amide	38	192.5—193 (decomp.)	59.64, 59.60	59.43	6.32, 6.38	6.35	12.40, 12.61	12.60
3-o-Tolylthiazolidine-2-carboxylic acid amide	21.5	155—155.5	59.06, 59.01	59.43	6.38, 6.58	6.35	12.30, 12.31	12.60
3-p-Anisylthiazolidine-2-carboxylic acid amide	27	162—163	55.84, 55.74	55.44	6.15, 5.96	5.92	12.08, 11.86	11.76
3-o-Anisylthiazolidine-2-carboxylic acid amide	25	149—150	55.25, 55.16	55.44	6.20, 6.19	5.92	11.85, 11.98	11.76

The 3-arylthiazolidine-2-carboxylic acid amides prepared in the present work are listed in Table 1.

3-Arylthiazolidine-2-carboxylic acid amides are soluble in acetone and dichloroethane, poorly soluble in alcohol, ether, and benzene, and insoluble in water.

Esters and Hydrazides of 3-Arylthiazolidine-2-carboxylic Acids

Ethyl-3-phenylthiazolidine-2-carboxylate. A mixture of 7.65 g (0.05 mole) of N-(β-mercaptoethyl)aniline, 11.8 g (0.075 mole) of ethyl dichloroacetate, 5 g (0.06 mole) of anhydrous sodium acetate, 7.5 g (0.066 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 5 hrs in a water bath.

After the alcohol was driven off, the solid residue, permeated with oil, was shaken in a separatory funnel with a mixture of water and ether until it was complete dissolved; the ether layer was drawn off, and the aqueous solution was then extracted with ether three more times. The combined extracts were dried with anhydrous magnesium sulfate.

After the ether was driven off, the dark-red oil was extracted for 12 hrs in an extractor with light petroleum ether (b. p. 30-50°). After the petroleum ether was driven off, there was obtained 6.05 g (51%) of a yellowish oil, which after distillation in vacuo in a current of nitrogen had the following constants:

B. p. 163-164° (2 mm), $n^{20}D$ 1.5795, d^{20}_4 1.1846, MR_D 66.62. $C_{12}H_{15}O_2NS F_3$. Calculated 65.38. Found %: C 61.08, 61.02; H 6.62, 6.69; N 5.65, 5.74. $C_{12}H_{15}O_2NS$. Caculated %: C 60.73; H 6.37; N 5.90.

Ethyl 3-p-tolylthiazolidine-2-carboxylate. Into reaction were brought 8.35 g of N-(β-mercaptoethyl)-p-toluidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other components of the mixture.

After the corresponding treatment of the reaction product an oil was obtained which partly crystallized on standing. The crystals — ethyl 3-p-tolylthiazolidine-2-carboxylate — were filtered out and were dissolved on heating in light petroleum ether (b. p. 30-50°); the filtrate was extracted with the latter in an extractor. The extracts obtained were combined, and after the solvent was driven off, a crystalline residue separated out; m. p. 57-57.5° (from alcohol). Yield, 5.2 g (41.5%).

Found %: C 62.08, 62.26; H 6.93, 6.80; N 5.61, 5.50. $C_{13}H_{17}O_2NS$. Calculated %: C 62.12; H 6.82; N 5.57.

Ethyl 3-o-tolylthiazolidine-2-carboxylate. Into reaction were brought 8.35 g of N-(β-mercaptoethyl)-o-toluidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other components of the mixture.

After the corresponding treatment of the reaction product, the following fractions were isolated on distillation in vacuo of the resulting oil in a current of nitrogen: 1st fraction, b. p. up to 125° (3 mm), 0.3 g; 2nd fraction, b. p. 160-167° (3 mm), 6.1 g (49%); residue – tar.

Fraction 1 was unchanged ethyl dichloroacetate. Fraction 2 – ethyl 3-o-tolylthiazolidine-2-carboxylate – was redistilled:

B. p. 164-165° (3 mm), $n^{20}D$ 1.5630, d^{25}_4 1.1515, MR_D 70.90. $C_{13}H_{17}O_2NS\digamma_3$. Calculated 70.00. Found %: C 62.78, 62.77; H 6.72, 6.88; N 5.35, 5.28. $C_{13}H_{17}O_2NS$. Calculated %: C 62.12; H 6.82; N 5.57.

Ethyl 3-p-anisylthiazolidine-2-carboxylate. When the oily product of the reaction of 9.15 g of N-(β-mercaptoethyl)-p-anisidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other reaction components was distilled in vacuo in a current of nitrogen at 176-180° (2 mm), a yellow oil was isolated, which partly crystallized on standing. The crystals – ethyl 3-p-anisylthiazolidine-2-carboxylate – were pressed out and recrystallized from alcohol; m. p. 48-48.5°. Yield, 4.01 g (30%).

Found %: C 58.56, 58.67; H 6.47, 6.65; N 5.13, 5.29. $C_{13}H_{17}O_3NS$. Calculated %: C 58.40; H 6.41; N 5.24.

Ethyl 3-o-anisylthiazolidine-2-carboxylate. When the product of the reaction of 9.15 g of N-(β-mercaptoethyl)-o-anisidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other reaction components was distilled in vacuo in a current of nitrogen, there was isolated 4.3 g (32.5%) of ethyl 3-o-anisylthiazolidine-2-carboxylate (yellow oil):

B. p. 180-181° (3 mm), $n^{20}D$ 1.5730, d^{20}_4 1.1885, MR_D 74.12. $C_{13}H_{17}O_3NS\digamma_3$. Calculated 71.64. Found %: C 59.27; H 6.70; N 5.42, 5.42. $C_{13}H_{17}O_3NS$. Calculated %: C 58.40; H 6.41; N 5.24.

3-Arylthiazolidine-2-carboxylic Acid Hydrazides

Procedure. A mixture of the ethyl 3-arylthiazolidine-2-carboxylate, hydrazine hydrate, and alcohol (taken in the ratio, 1 g of the ester to 1 ml of hydrazine hydrate and 1 ml of alcohol) was boiled for 10 min, until a clear solution was obtained. The 3-arylthiazolidine-2-carboxylic acid hydrazide crystals, which separated out

TABLE 2

Hydrazides	Yield in %	Melting point	C (%)		H (%)		N (%)	
			found	calc.	found	calc.	found	calc.
3-Phenylthiazolidine-2-carboxylic acid hydrazide	76	135.5—136°	53.50, 53.58	53.79	5.92, 5.98	5.87	18.72, 18.60	18.82
3-p-Tolylthiazolidine-2-carboxylic acid hydrazide	100	176—176.5	55.65, 55.88	55.67	6.39, 6.38	6.37	17.54, 17.50	17.71
3-o-Tolylthiazolidine-2-carboxylic acid hydrazide	74	130.5—131	55.91, 55.77	55.67	6.21, 6.15	6.37	17.80, 17.85	17.71
3-p-Anisylthiazolidine-2-carboxylic acid hydrazide	100	143.5—144	51.90, 51.93	52.15	6.06, 6.02	5.97	16.16, 16.32	16.59
3-o-Anisylthiazolidine-2-carboxylic acid hydrazide	70	103—104	52.26, 52.07	52.15	6.08, 5.79	5.97	16.55, 16.54	16.59

on cooling, were filtered off; several milliliters of water was added to the filtrate, and the crystals, which precipitated were again filtered off. The crystals were washed with ether, dried, and recrystallized from water.

The 3-arylthiazolidine-2-carboxylic acid hydrazides, prepared in the present work, are listed in Table 2.

3-Arylthiazolidine-2-carboxylic acid hydrazides are soluble in alcohol, benzene, acetone, and dichloroethane; they are insoluble in ether and water.

SUMMARY

1. The reaction of N-(β-mercaptoethyl)arylamines with dichloroacetic acid leads to 3-arylthiazolidine-2-carboxylic acids, which are not described in the literature. In the present work 3-phenyl-, 3-p-tolyl-, and 3-p-anisylthiazolidine-2-carboxylic acids were prepared in this way.

2. The condensation of N-(β-mercaptoethyl)arylamines with dichloroacetamide, which takes a similar course, leads to 3-arylthiazolidine-2-carboxylic acid amides, which are not described in the literature. In the present work 3-phenyl-, 3-p-tolyl-, 3-o-tolyl-, 3-p-anisyl-, and 3-o-anisylthiazolidine-2-carboxylic acid amides were prepared in this way.

3. The condensation of N-(β-mercaptoethyl)arylamines with ethyl dichloroacetate leads to the ethyl esters of 3-phenyl-, 3-p-tolyl-, 3-o-anisylthiazolidine-2-carboxylic acids, which are not described in the literature; the esters are converted to the corresponding hydrazides on treatment with hydrazine hydrate.

LITERATURE CITED

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Received March 14, 1957

Moscow State University

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* Original Russian pagination. See C. B. translation.

REACTION OF 1,3-DICHLOROBUTENE-2 WITH ISOPRENE AND DIVINYL UNDER THE INFLUENCE OF $FeCl_3$. III

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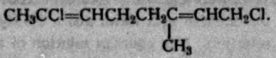
The results of a study of the reaction of 1,3-dichlorobutene-2 with chloroprene under the influence of Friedel-Crafts-Gustavson catalysts were given in the preceding report.[*] Continuing the work in the same direction, we studied the reaction of 1,3-dichlorobutene-2 with isoprene and divinyl in the presence of $FeCl_3$. In both cases the formation of products of low molecular weight, as well as resinous products, was observed.

We attempted to use $AlCl_3$, also, as catalyst; however, it was impossible to isolate the primary product in this case. Subsequent experiments, therefore, were conducted only with $FeCl_3$ catalyst at a concentration not exceeding 0.25 mole%, since at greater concentrations the amount of products of high molecular weight increased with simultaneous decrease of the yield of the primary addition product, which hindered the isolation of the latter.

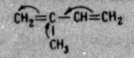
Both in reactions with isoprene and in reaction with divinyl, the composition of the products is strongly affected by the ratio of the initial substances, the yield of the primary addition product increasing with increase in the excess of 1,3-dichlorobutene-2.

As a consequence of the addition of 1,3-dichlorobutene-2 to isoprene, the formation of 6 reaction products, depending on the course of the addition: 1,4; 4,1; 1,2; 2,1; 3,4; or 4,3; may be expected as the primary result. It was found that addition takes place mainly in the 1,4-position with formation of compound (I).



$$CH_3CCl{=}CHCH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CHCH_2Cl.$$

(I)



(II)

The structure of the product formed was proved by ozonization. Among the decomposition products of the ozonide were found acetic (72.63%), chloroacetic (82.17%), and levulinic (85.7%) acids and tars.

It follows from the ozonolysis data that 1,3-dichlorobutene-2 adds to isoprene mainly in the 1,4-position (Formula I), which is also in accord with the distribution of electron density in the isoprene molecule (II).

On the basis of such an electron density distribution in the isoprene molecule it could be assumed that the addition of the complex $CH_3CCl{=}CHCH_2^+ \cdot FeCl_4^-$ to isoprene would take place mainly in the 1,4-position with formation of compound (I); other courses are less probable.

Products of the addition of two molecules of 1,3-dichlorobutene-2 to one of isoprene were not found in the reaction mixture.

The polymers were divided into narrow fractions by precipitating them with methyl alcohol from benzene solution. The isolated fractions were characterized by their molecular weight, and also by analysis for total chlorine and saponifiable chlorine. Their structures were not determined, owing to their complexity.

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[*] J. Gen. Chem. 28, 574 (1958). [Original Russian pagination. See C.B. Translation.

The presence of saponifiable chlorine, established by analyses of individual fractions, gives grounds for assuming that the polymer is formed by stepwise condensation from one 1,3-dichlorobutene-2 molecule and n molecules of isoprene. Here telomerization also takes place, as in the case of the reaction of 1,3-dichlorobutene-2 with chloroprene.

As a consequency of the addition of 1,3-dichlorobutene-2 to divinyl the formation of three different reaction products, depending on the course of the addition (1,4, 1,2, or 2,1), may be expected as the primary result. The method of ozonolysis was used to establish the structure. Among the decomposition products of the ozonide were found acetic (72.4%), chloroacetic (71.8%), and succinic (75.2%) acids. The ozonolysis data show that the addition of 1,3-dichlorobutene-2 to divinyl, also, occurs mainly in the 1,4-position with formation of the compound $CH_3CCl=CHCH_2CH_2CH=CHCH_2Cl$.

As in the case of isoprene, products of the addition of two molecules of 1,3-dichlorobutene-2 to one of divinyl were not found in the reaction mixture.

The results of the investigation confirmed that, as in the cases of chloroprene and isoprene, telomerization also occurs here with formation of compounds of higher molecular weight.

EXPERIMENTAL

1. Reaction of 1,3-Dichlorobutene-2 with Isoprene

In the presence of 0.487 g of $FeCl_3$ (0.25 mole%), 122.2 g of 1,3-dichlorobutene-2 and 16.4 g of isoprene were kept at 20° in a round-bottomed flask with a reflux condenser in a nitrogen atmosphere for 6 hrs. In the course of the work it turned out that, owing to the exothermic character of the polycondensation reaction, the temperature rose and resinification occurred. The reaction product was washed with dilute hydrochloric acid and then water, and dried with Na_2SO_4, after which the unreacted starting materials were driven off. The residue was distilled in vacuo. One fraction, b. p. 65-75° at 3 mm (4.69 g), and a residue (polymer, 8.2 g) were obtained thereby. By redistillation of this fraction, 3.07 g of product was obtained.

B. p. 70-72° at 3 mm, d^{20}_4 1.0578, $n^{20}D$ 1.4887, MR_D 52.72; calculated 52.56. Found %: Cl 36.36, sapon. Cl 18.17. M 187; bromine number 167.7. $C_9H_{14}Cl_2$. Calculated %: Cl 36.79, sapon. Cl 18.39. M 193; bromine number 165.8.

Corresponding fractions from several experiments were combined and ozonized. For ozonization 7.72 g of the product was taken. After decomposition of the ozonide with water and a 3% H_2O_2 solution the acid mixture did not contain formic acid (test with $AgNO_3$ solution). The aqueous solution of acids was filtered to remove tars (0.921 g). After distillation of the volatile acids in vacuo (at 35-40°), a tarry, crystalline product (4.78 g) remained in the flask.

Hydrochloric acid was determined from the chlorine content in the volatile-acid mixture.

Found 1.228 g (84.17%) HCl.

The acetic acid was isolated as the silver salt by treatment of the distilled volatile-acid solution with silver oxide; after recrystallization the salt was analyzed.

Found %: Ag 63.98. $C_2H_3O_2Ag$. Calculated %: Ag 64.59.

The quantity of acetic acid was calculated from the total acidity of the volatile-acid mixture, since no other acids were found in the form of the silver salts. For neutralization of the volatile acids 3.51 g of KOH was required; 1.883 g of this was used to neutralize hydrochloric acid; hence 1.627 g of KOH was used for neutralization of acetic acid, which corresponds to 1.743 g (72.63%) of acetic acid.

The chloroacetic acid, isolated from the crystalline distillation residue, had b. p. 67-69° at 4 mm and m. p. 58-59° (according to literature data, m. p. 61.5°).

Found %: Cl 36.35. Equiv.: 603.14. $C_2H_3O_2Cl$. Calculated %: Cl 37.57. Equiv.: 592.6.

The quantity of chloroacetic acid (82.17%) was calculated from the chlorine content in the crystalline product (1.36 g, which corresponds to 3.62 g of chloroacetic acid).

The levulinic acid, which was also isolated from the crystalline residue, distilled with decomposition (b. p. 80-85° at 4 mm); its crystals melted at 34-35° (according to literature data, m. p. 33.5°).

Found: equiv. 465.37. $C_5H_8O_3$. Calculated: equiv. 482.30.

The quantity of levulinic acid was calculated from the total acidity of the aqueous solution. For neutralization of the latter, 5.655 g of KOH was required; of this the neutralization of hydrochloric acid used 1.863 g, that of acetic acid used 1.627 g, and that of chloroacetic acid used 2.145 g. Since no other acids were found, the rest of the KOH (1.961 g) was consumed by levulinic acid, the calculated quantity of which was 3.98 g (85.7%).

Study of polymers. By stepwise addition of methyl alcohol to a benzene solution containing 36.7 g of the polymer, 4 fractions were obtained, the analytical data for which are given in the table.

Physicochemical Constants of Polymeric Fractions

No. of fraction	Weight of fraction		Average molecular wt. (cryoscopic determination in benz.)		Total chlorine (in %)		Saponifiable chlorine (in %)		Calculated empirical formula
	in g	in %	found	calc.	found	calc.	found	calc.	
1	7.03	19.24	1345.2	1417	4.27	5.01	2.18	2.5	$C_{99}H_{158}Cl_2$
2	19.34	52.51	842.7	873	7.48	8.13	3.68	4.07	$C_{59}H_{88}Cl_2$
3	6.03	16.51	568.2	533	12.62	13.21	6.02	6.66	$C_{31}H_{5}\,Cl_2$
4	4.30	11.74							Mixture of dimers and trimers

2. Reaction of 1,3-Dichlorobutene-2 with Divinyl

In the presence of 0.25 g of $FeCl_3$ (0.75 mole%), 62.5 g of 1,3-dichlorobutene-2 and 13.8 g of divinyl were kept in a sealed ampoule in a nitrogen atmosphere at 20° for 20 hrs. The reaction product was washed with 10% hydrochloric acid and water in order to remove the catalyst, dried with $CaCl_2$, and then distilled. After the unreacted starting materials were driven off, the residue was distilled in vacuo. One fraction, b. p. 65-78° at 10 mm (4.1 g), and a residue (polymer, 5.8 g) were obtained thereby. By redistillation of this fraction, 2.75 g of product was obtained.

B. P. 74-76° at 10 mm, d^{20}_4 1.0737, $n^{20}D$ 1.4780, MR_D 47.22; calculated 47.94. Found %: Cl 39.2, sapon. Cl 19.6. M 167.0; bromine number 180.2. $C_8H_{12}Cl_2$. Calculated %: Cl 39.67, sapon. Cl 19.83. M 179; bromine number 181.

Corresponding fractions from several experiments were combined and ozonized. For ozonization 4.22 g of the product was taken. After decomposition of the ozonide with water and a 3% H_2O_2 solution the acid mixture did not contain formic acid (test with $AgNO_3$ solution).

After the volatile acids were distilled off in vacuo at 45-50° (35-40 mm), tarry crystals (3.5 g) remained in the flask. The hydrochloric acid in the volatile-acid mixture was determined from the chloride-ion content. There was found 0.51 g (60%) of HCl.

An aliquot part of the volatile-acid solution was treated with freshly precipitated silver oxide, the AgCl precipitate was filtered off, and the filtrate was evaporated in vacuo. The acetic acid was thereby isolated as the silver salt, which after recrystallization was analyzed.

Found %: Ag 63.84. $C_2H_3O_2Ag$. Calculated %: Ag 64.58.

No other acids were found in the form of the silver salts. For neutralization of the volatile acids, 1.74 g of KOH was required; of this the neutralization of hydrochloric acid used 0.784 g, and that of acetic acid used 0.956 g, which corresponds to 1.024 g (72.4%) of acetic acid.

The chloroacetic acid (b. p. 69-70° at 5 mm) was isolated from the crystalline residue by distillation in vacuo in the form of white crystals, m. p. 60-62°.

Found %: Cl 37.07. Equiv. 597.8. $C_2H_3O_2Cl$. Calculated %: Cl 37.56. Equiv. 592.6.

The quantity of chloroacetic acid was calculated from the chlorine content in the entire crystalline product (0.6 g), which corresponds to 1.6 g (71.8%) of chloroacetic acid.

The residual crystals from the distillation had m. p. 179-181° after recrystallization. For succinic acid, according to literature data, the m. p. is 182.3°. A mixture test with pure succinic acid gave no melting-point depression.

Found: equiv. 923.4. $C_4H_6O_4$. Calculated: equiv. 949.15.

The quantity of succinic acid was calculated from the total acidity of the aqueous solution. For neutralization 4.72 g of KOH was required; of this the neutralization of hydrochloric, acetic, and chloroacetic acids used 2.69 g; that of succinic acid (by difference) consumed 2.035 g of KOH, which corresponds to 2.145 g (75.24%) of succinic acid.

SUMMARY

1. The reaction of 1,3-dichlorobutene-2 with isoprene and divinyl in the presence of $FeCl_3$ has been investigated.

2. It has been found that in the reaction of 1,3-dichlorobutene-2 with isoprene and divinyl, both resinous substances of high molecular weight and primary addition products of low molecular weight are formed.

3. 1,7-Dichloro-3-methyloctadiene-2,6 – the product of addition of 1,3-dichlorobutene-2 to isoprene in the 1,4-position – has been isolated.

4. 1,7-Dichlorooctadiene-2,6 – the product of addition of 1,3-dichlorobutene-2 to divinyl in the 1,4-position – has been isolated.

Received March 25, 1957

1,4-HYDROXYKETONES AND 1,4-DIKETONES IN THE CATALYTIC SYNTHESIS OF HOMOLOGS OF Δ^2-PYRROLINE AND Δ^2-DIHYDROTHIOPHENE, AND, CORRESPONDINGLY, HOMOLOGS OF PYRROLE AND THIOPHENE

Iu. K. Iur'ev and N. V. Makarov

In 1938 it was shown by one of us that on dehydration of butanediol-1,4 in the presence of alumina, furanidin (tetrahydrofuran) is formed, while on joint dehydration with ammonia and with hydrogen sulfide in the presence of alumina at 400°, pyrrolidine and thiophane, respectively, are obtained [1]; the joint catalytic dehydration of butanediol-1,4 with aniline in the presence of aluminosilicate at 330° [2] or activated alumina at 275° leads to N-phenylpyralidine.

It was also shown by one of us that the catalytic dehydration of cis-butene-2-diol-1,4 leads to Δ^3-dihydrofuran, while on joint catalytic dehydration of this diol and aniline in the presence of activated alumina at 350°, 1-phenyl-Δ^3-pyrroline is obtained [3]; similarly, on catalytic dehydration of butyne-2-diol-1,4, furan is obtained, while on joint catalytic dehydration with ammonia, with aniline, and with hydrogen sulfide at 400°, pyrrole, N-phenylpyrrole, and thiophene, respectively, are obtained [3].

The range of the reactions given above is widened by the latest instances of the catalytic dehydration of 1,4-diols of the types

$$\mathrm{RR'C(OH)C{\equiv}CC(OH)R''R'''};\quad \mathrm{RR'C(OH)CH{=}CHC(OH)R''R'''},$$
$$\mathrm{RR'C(OH)CH_2{-}CH_2C(OH)R''R'''},$$

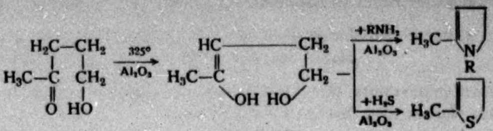
which leads to the formation of substituted furans, dihydrofurans, and furanidins, respectively [4], and also by instances of joint catalytic dehydration of the stated diols with ammonia and with alkyl- or arylamines with formation of N-substituted pyrroles, Δ^3-pyrrolines, or pyrrolidines, respectively [5-7]. Both alumina and alumina activated with various metal oxides were used as catalysts in these reactions [4-8].

Thus, into the catalytic synthesis of compounds with five-membered heterocyclic rings, both saturated and unsaturated 1,4-diols were introduced, the double or triple bond of the latter occupying a central position between the second and third carbon atoms in this system of four carbon atoms.

In connection with this, it was of interest to introduce into the described synthesis the simplest 1,4-hydroxyketone, and also the simplest 1,4-diketone, which on joint catalytic dehydration with ammonia, amines, or hydrogen sulfide must react in the enol forms as unsaturated diols with one and two hydroxyl groups, respectively, attached to doubly-bonded carbon atoms.

In the present work, as a representative 1,4-dihydroxyketone, we used γ-acetylpropyl alcohol, which, reacting in the enol form as pentene-2-diol-2,5, gave 2-methyl-Δ^2-pyrroline (50%) on treatment with ammonia in the presence of alumina at an elevated temperature, 1-phenyl-2-methyl-Δ^2-pyrroline (58%) on treatment with aniline, and 2-methyl-Δ^2-dihydrothiophene (38.5%) on treatment with hydrogen sulfide [9] (see diagram on next page).

Let us note that in the reaction with ammonia, increase in the rate of passage of γ-acetylpropyl alcohol over alumina from 0.45 to 0.8 ml/min and 1.6 ml/min led to decrease in the yield of 2-methyl-Δ^2-pyrroline and the appearance of ever-increasing quantities of 2-methyl-Δ^2-dihydrofuran. The latter resulted from the



(R = H. C_6H_5)

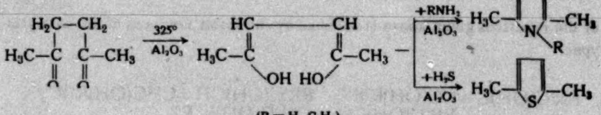
intramolecular catalytic dehydration of pentene-2-diol-1,4 – the enolization product of γ-acetylpropyl alcohol – which obviously proceeded at a higher rate than the joint catalytic dehydration with ammonia.

This also indicates that in the reactions described by us, elimination of water and closing of the nitrogen- or sulfur-containing ring take place directly through joint catalytic dehydration of ammonia, amines, or hydrogen sulfide and 1,4-diols, as well as 1,4-hydroxyketones (see below) in their enol forms.

Therefore, the formation of 2-methyldihydrofuran is not an obligatory intermediate stage in the catalytic synthesis of 2-methyl-Δ^2-pyrroline from γ-acetylpropyl alcohol and ammonia. With a definite reagent ratio and contact time the oxygen-containing heterocyclic compounds formed as by-products must be converted to the corresponding nitrogen-containing heterocyclic compounds by the reaction described by one of us [10], but at a lower rate, owing to the greater complexity of the process.

The joint catalytic dehydration of γ-acetylpropyl alcohol and aniline in the presence of aluminosilicate also led to 1-phenyl-2-methyl-Δ^2-pyrroline.

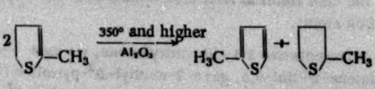
When acetonylacetone was introduced into the catalytic synthesis, we obtained 2,5-dimethylpyrrole (36%) on treatment with ammonia in the presence of alumina at an elevated temperature, 1-phenyl-2,5-dimethylpyrrole (43%) on treatment with aniline, and 2,5-dimethylthiophene (35%) on treatment with hydrogen sulfide [9].



(R = H, C_6H_5)

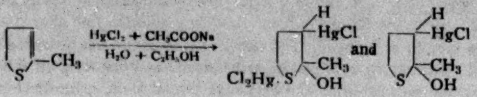
The preparation of this homolog in 35% yield by the joint catalytic dehydration of the 1,4-diketone (reacting in its enol form) and hydrogen sulfide shows how easily a reaction of this type occurs and how much simpler is the scheme which it follows, in comparison with the preparation of thiophene homologs by the catalytic conversion of furan homologs. In the latter case, on treatment of silvan with hydrogen sulfide in the presence of alumina, the yield of 2-methylthiophene did not exceed 10%, while 2,5-dimethylfuran, on treatment with hydrogen sulfide, was so strongly decomposed that only traces of 2,5-dimethylthiophene were obtained [11].

It should be particularly noted that the synthesis of 2-methyl-Δ^2-dihydrothiophene by the joint catalytic dehydration of γ-acetylpropyl alcohol and hydrogen sulfide goes relatively smoothly at 325° but by 350° appreciable amounts of 2-methylthiophene and 2-methylthiophane – products of the irreversible catalysis of 2-methyl-Δ^2-dihydrothiophene – appear in the reaction product together with the latter.



Thus we have obtained a direct proof of the fact that, like other incomplete hydrides of compounds of aromatic nature, dihydrothiophene and its homologs are subject to N. D. Zelinskii's irreversible catalysis [12]. This was first established by one of us in the study of the catalytic conversion of dihydrofuran under the influence of hydrogen sulfide, the product of which proved to be a mixture of thiophene and thiophane.

On mercuration of 2-methyl-Δ^2-dihydrothiophene by the Steinkopf method [14] – treatment with mercuric chloride in aqueous-alcoholic solution in the presence of sodium acetate – we obtained 1-dichloromercuri-2-methyl-2-hydroxy-3-chloromercurithiophane together with a small amount of 2-methyl-2-hydroxy-3-chloromercurithiophane.



EXPERIMENTAL

2-Methyl-Δ^2-pyrroline. Acetylpropyl alcohol was passed through a tube, filled with alumina (internal diameter of tube, 23 mm; length of catalyst layer, 40 cm), in a strong current of ammonia at a rate from 0.3 to 0.45 ml/min in the interval 275-350°.

The catalyzate obtained in the first receiver was saturated with solid potassium hydroxide and extracted with ether. In the second receiver, which was cooled with solid carbon dioxide and alcohol, the ammonia and the catalysis product, partly entrained by it, were condensed. After careful evaporation of the ammonia from a flask with a reflux condenser the residue was combined with the main mass of reaction product. After drying with potassium hydroxide and driving off the ether, the reaction products was distilled over sodium from a flask with a fractionating column, 2-methyl-Δ^2-dihydrofuran being collected at 79-82° and 2-methyl-Δ^2-pyrroline at 103-105°.

The results obtained in these experiments are given in Table 1.

TABLE 1

No. of expt.	Quantity of γ-acetylpropyl alcohol (in g)	Rate of introduction (ml/min)	Temperature of experiment	Yield of 2-methyl-Δ^2-pyrroline (in %)	Yield of 2-methyl-Δ^2-dihydrofuran (in %)
1	10.0	0.3	275°	12.0	—
2	10.0	0.3	300	18.5	—
3	10.0	0.3	325	24.0	—
4	10.0	0.3	350	18.5	—
5	10.0	0.35	325	38.0	—
6	10.0	0.45	325	50.0	—
7	18.0	0.8	325	18.5	16.0
8	18.0	1.6	325	10.5	31.0

From the data given in Table 1, it is evident that when acetylpropyl alcohol was introduced at a rate of 0.3 ml/min, the yield of 2-methyl-Δ^2-pyrroline increased from 12 to 24% as the reaction temperature rose from 275 to 325°, but decreased to 18.5% at 350°.

When the rate of introduction of the alcohol was increased to 0.45 ml/min at 325°, the yield of 2-methyl-Δ^2-pyrroline rose to 50%, but on further increase of the rate the yield of the latter fell, and ever-increasing amounts of 2-methyl-Δ^2-dihydrofuran appeared in the reaction product.

2-Methyl-Δ^2-pyrroline, combined from all experiments, after redistillation had the following constants:

B. p. 104-105° (756 mm), $n^{20}D$ 1.4356, d^{20}_4 0.8843, MR_D 26.00. $C_5H_9N\ulcorner$. Calculated 26.18. Found %: C 72.54, 72.35; H 10.76, 10.86; N 16.91, 16.98. C_5H_9N. Calculated %: C 72.24; H 10.91; N 16.85.

2-Methyl-Δ^2-pyrroline picrate was obtained by mixing ethereal solutions of the base and of picric acid; m. p. 124°(from water).

Found %: N 17.80. $C_{11}H_{12}O_7N_4$. Calculated %: N 17.97. Literature data: b. p. 50-51° (110-116 mm), d^{22}_4 0.8995 [15], b. p. 90-91° (750 mm) [16], b. p. 105-110° [17].

The 2-methyl-Δ^2-dihydrofuran obtained in Experiments 7 and 8 was combined and redistilled over sodium:

B. p. 80-81° (750 mm), $n^{20}D$ 1.4089, d^{20}_4 0.8890, MR_D 22.70. C_5H_8O F. Calculated 22.83. Found %: C 71.31, 71.26; H 9.49, 9.53. C_5H_8O. Calculated %: C 71.39; H 9.58. Literature data: b. p. 75° [18], b. p. 82°, d^{20}_{20} 0.9062 [19].

1-Phenyl-2-methyl-Δ^2-pyrroline. Mixtures of γ-acetylpropyl alcohol and freshly distilled aniline in the molar ratios 1:1 and 1:2 were passed through a tube containing alumina (see above) at 330° and at rate of 0.3 to 0.6 ml/min in a slow current of nitrogen. The catalyzate obtained was saturated with potassium hydroxide and extracted with ether. After drying with potassium hydroxide and distilling off the ether and unchanged aniline (b. p. 48-49° at 1 mm), the reaction product – 1-phenyl-2-methyl-Δ^2-pyrroline – was collected at 85-87° (1 mm). The results obtained in these experiments are given in Table 2.

TABLE 2

No. of expt.	Quantity of acetylpropyl alcohol (in g)	Quantity of aniline (in g)	Molar ratio of reagents	Temperature of expt.	Rate of introduction of mixture (ml/min)	Yield of 1-phenyl-2-methyl-Δ^2-pyrroline (in %)
1	10.2	9.8	1 : 1	325°	0.4	24
2	10.2	19.6	1 : 2	330	0.4	52
3	5.2	9.8	1 : 2	330	0.3	58
4	5.2	9.8	1 : 2	330	0.5	50
5	5.2	9.8	1 : 2	330	0.6	45

From the data of Table 2, it is evident that the optimum conditions for preparing 1-phenyl-2-methyl-Δ^2-pyrroline (58% yield) are 330°, a molar ratio of acetylpropyl alcohol : aniline = 1 : 2 in the mixture and a rate of passage of the latter over the catalyst, equal to 0.3 ml/min.

1-Phenyl-2-methyl-Δ^2-pyrroline, after redistillation in a current of nitrogen, had the following constants:

B. p. 85-86° (2 mm), $n^{20}D$ 1.5762, d^{20}_4 1.0220, MR_D 45.67. $C_{11}H_{13}N$ F_4. Calculated 45.80. Found %: C 83.22, 83.37; H 8.46, 8.31; N 8.65, 8.62. $C_{11}H_{13}N$. Calculated %: C 83.00; H 8.24; N 8.79.

1-Phenyl-2-methyl-Δ^2-pyrolline picrate was obtained by mixing ethereal solutions of the base and of picric acid; m. p. 95° (from water).

Found %: N 14.46. $C_{17}HO_{16}O_7N_4$. Calculated %: N 14.40.

2-Methyl-Δ^2-dihydrothiophene. In each experiment 10 g of acetylpropyl alcohol was passed at a rate of 0.4 ml/min in a current of hydrogen sulfide through a tube filled with alumina (see above) and heated to 325°. The catalyzate was saturated with potassium hydroxide and extracted with ether. The other extract was dried with potassium hydroxide. After the ether was driven off, the residue was distilled over sodium from a flask with a fractionating column, a broad fraction being collected in the interval 105-135° at 756 mm (the main mass passed over at 128-129°); above 135°, obvious decomposition and resinification of the residue began.

TABLE 3

No. of fraction	Boiling point (743 mm)	Quantity (in ml)	n^{20}_D	d^{20}_4
1	105 —109.5°	4.3	1.4701	0.9545
2	109.5—128.5	3.3	1.5009	0.9877
3	128.5—129.5	12	1.5071	0.9906
4	129.5—130.5	16	1.5073	0.9900
5	130.5—131.5	2	1.5065	0.9847

In all, 6 experiments were conducted and 45 g of the stated fraction was obtained. On distillation of the latter through a column (18 theoretical plates), fractions were isolated, the constants of which are given in Table 3.

On redistillation of the third and fourth fractions, there was obtained 23 ml (22.8 g) (38.5%) of 2-methyl-Δ^2-dihydrothiophene:

B. p. 129-130° (745 mm), $n^{20}D$ 1.5073, d^{20}_4 0.9902, MR_D 29.83. C_5H_8S F. Calculated 29.45. Found %: C 59.95, 59.87; H 7.89, 7.94; S 31.87, 31.95. C_5H_8S. Calculated %: C 60.00; H 8.00; S 32.00.

On treatment of 1 g of 2-methyl-Δ^2-dihydrothiophene with a solution of 2.6 g of mercuric chloride and 3 g of sodium acetate in 80 ml of alcohol, diluted with 60 ml of water [14], 1-dichloromercuri-2-methyl-2-hydroxy-3-chloromercurithiophane was obtained; m. p. 143° (from alcohol).

Found %: Hg 64.00, 64.49. $C_5H_9OSCl_3Hg_2$. Calculated %: Hg 64.32.

Crystals of 2-methyl-2-hydroxy-3-chloromercurithiophane separated out from the mother liquor on standing.

Found %: Hg 56.42, 56.50. $C_5H_9OSClHg$. Calculated %: Hg 56.62.

Experiments on the catalytic synthesis of 2-methyl-Δ^2-dihydrothiophene from acetylpropyl alcohol (10 g in each experiment) were also conducted at 350°.

On distillation through a column (18 theoretical plates) of 6 g of the fraction with b. p. 105-135°, isolated from the catalyzates of two experiments of this series, besides 2-methyl-Δ^2-dihydrothiophene there were obtained:

a) 0.82 g of 2-methylthiophene; b. p. 110.5° (750 mm), $n^{20}D$ 1.5240, d^{20}_4 1.0200, MR_D 31.00. C_5H_6S F_2. Calculated 30.70. Literature data: b. p. 112-113°, $n^{20}D$ 1.5210, d^{20}_4 1.0168 [20].

By the mercuration of 2-methylthiophene, 2-methyl-5-chloromercurithiophene was obtained; m. p. 200° (from alcohol).

Found %: Hg 60.08. C_5H_5SClHg. Calculated %: Hg 60.18. Literature data: b. p. 197° [21], 202° [14].

b) 0.96 g of 2-methylthiophene; b. p. 131-132° (750 mm), $n^{20}D$ 1.4982, d^{20}_4 0.9577, MR_D 31.10. $C_5H_{10}S$. Calculated 31.30. Literature data: b. p. 131.2-132° (756 mm), $n^{20}D$ 1.4922, d^{20}_4 0.9577 [22].

2,5-Dimethylpyrrole. In each experiment 10 g of acetonylacetone was passed over alumina at 325° at a rate of 0.4 ml/min in a strong current of ammonia. After the appropriate treatment of the catalyzates from two experiments and distillation of the reaction product, there was obtained 6 g (36%) of 2,5-dimethylpyrrole:

B. p. 165-166° (759 mm), $n^{20}D$ 1.5028, d^{20}_4 0.9288, MR_D 30.25. C_6H_9N F_2. Calculated 30.37. Found %: N 14.84, 14.89. C_6H_9N. Calculated %: N 14.73.

At 350° the yield of 2,5-dimethylpyrrole fell to 30%.

Literature data: b. p. 165° (740 mm) [23], 166.5 (756 mm), $n^{19.8}D$ 1.5036, $d^{19.8}_4$ 0.9353 [24]; b. p. 170-172° (765 mm), $n^{20}D$ 1.5028, d^{20}_4 0.9344 [25].

1-Phenyl-2,5-dimethylpyrrole. A mixture of 6 g of acetonylacetone and 9.5 g of aniline (molar ratio 1 : 2) was passed over alumina at 325° at a rate of 0.35 ml/min in a slow current of nitrogen. After the appropriate treatment of the catalyzates from two experiments and distillation of the reaction product, there was obtained 13 g (43%) of 1-phenyl-2,5-dimethylpyrrole; m. p. 52-52.5°.

Found %: N 8.25, 8.29. $C_{12}H_{13}N$. Calculated %: N 8.18. Literature data: b. p. 252°, m. p. 51-52° [26]; m. p. 52-53° [25].

2,5-Dimethylthiophene. Acetonylacetone was passed over alumina at a rate of 0.4 ml/min in a strong current of hydrogen sulfide at 275, 325, and 350°. The catalyzate was treated as described under 2-methyl-Δ^2-dihydrothiophene. On distillation of the catalysis product, 2,5-dimethylthiophene was collected at 133-135°. The results obtained in these experiments are given in Table 4.

After redistillation of all the 2,5-dimethylthiophene over sodium, it had the following constants:

B. p. 134-135° (759 mm), $n^{20}D$ 1.5045, d^{20}_4 0.9775, MR_D 43.61. C_6H_8S F_2. Calculated 43.52. Found %: C 64.09, 64.17; H 7.21, 7.10; S 28.49, 28.47. C_6H_8S. Calculated %: C 64.23; H 7.18; S 28.57. Literature

TABLE 4

No. of expt.	Quantity of acetonylacetone (in g)	Temperature of expt.	Rate of introduction (ml/min)	Yield of 2,5-dimethylthiophene, %	n_D^{20}	d_4^{20}
1	10	275°	0.4	16.5	1.5046	0.9780
2	10	325	0.4	35.0	1.5040	0.9778
3	10	350	0.4	33.0	1.5043	0.9775

data: b. p. 134-135°, d^{19}_4 0.9755 [27], b. p. 136.5-137.3°, $d^{17.5}$ 0.9755 [28]; b. p. 135.5-136° (754.3 mm), $n^{19}D$ 1.51418, d^{19}_4 0.9858 [24].

2,5-Dimethyl-3-chloromercurithiophene melted at 187°.

Found %: Hg 57.69. C_6H_7SClHg. Calculated %: Hg 57.77. Literature data: b. p. 186° [14].

SUMMARY

1,4-Hydroxyketones and 1,4-diketones may well be used in the catalytic synthesis of heterocyclic compounds having a five-membered nitrogen- or sulfur-containing nucleus; the joint catalytic dehydration of γ-acetylpropyl alcohol with ammonia, with aniline, and with hydrogen sulfide in the presence of alumina at 325-330° is a good method of synthesis of 2-methyl-Δ^2-pyrroline, 1-phenyl-2-methyl-Δ^2-pyrroline, and 2-methyl-Δ^2-dihydrothiophene, respectively; on joint catalytic dehydration of acetonylacetone with ammonia, with aniline and with hydrogen sulfide in the presence of alumina at 325°, 2,5-dimethylpyrrole, 1-phenyl-2,5-dimethylpyrrole, and 2,5-dimethylthiophene, respectively, are obtained.

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Received March 20, 1957

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HETEROCYCLIC DERIVATIVES OF METHYL KETONES

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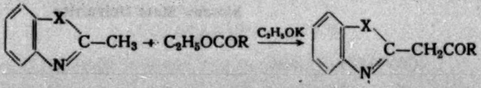
Many nitrogen heterocyclics containing a methyl group adjacent to the nitrogen atom readily undergo electrophilic substitution reactions. This is also true in condensation with esters.

In 1898 Wislicenus [1] condensed oxalic ester with quinaldine to prepare a substituted ester of pyruvic acid. Later on this reaction was studied in more detail by Borsche et al. [2], who extended it to other heterocyclics [3]. Diethyl oxalate is one of the most active acylating esters in condensations of this type. It seemed interesting to study this condensation with less active components also, such as ethyl benzoate and other esters.

In the presence of potassium ethoxide, ethyl benzoate reacts with 2-methyl homologs of various heterocyclics to form ketones by the scheme

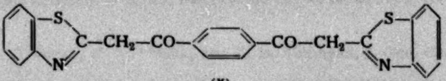


(I) $X = S$, $R = C_6H_5$; (II) $X = O$, $R = C_6H_5$; (III) $X = Se$, $R = C_6H_5$; (IV) $X = CH = CH$, $R = C_6H_5$; (V) $X = NCH_3$, $R = C_6H_5$; (VI) $X = S$, $R = CH_3$; (VII) $X = S$, $R = p\text{-}CH_3OC_6H_4$; (VIII) $X = S$, $R = p\text{-}ClC_6H_4$; (IX) $X = S$, $R = p\text{-}C_2H_5OCOC_6H_4$.

2-Methylbenzimidazole is an exception and does not react at all under these conditions. The yield of ketone obtained varies from 5 to 28% depending on the part of the heterocyclic X. If the various possibilities for the latter are arranged according to the increasing activity of the heterocyclic, we obtain the following series: $NH < Se < NCH_3 < CH{=}CH < O < S$, which agrees in general with the order of the decreasing basicity of the corresponding heterocyclics, determined from their other properties [4]. Benzselenazole is an exception, but this may be explained by the presence of side reactions during its condensation with ethyl benzoate.

One of the ketones which we prepared, ω-benzoyl-2-methylbenzthiazole (I), was described previously by Rogers and Sexton, who prepared it by another method [5].*

Para-substituted ethyl benzoates were noticeably more active in the reaction with 2-methylbenzthiazole. Thus, ethyl p-methoxybenzoate formed the corresponding ketone (VII) in 45% yield, ethyl p-chlorobenzoate gave 56% of (VIII) and diethyl terephthalate a 79% yield. In the latter case, about 2% of the diketone (X) was formed in addition to ω-(p-carbethoxybenzoyl)-2-methylbenzthiazole (IX).



(X)

The ketoester (IX) may be readily hydrolyzed to form the corresponding acid.

Ethyl acetate is less active in a condensation with 2-methylbenzthiazole and the reaction yielded only about 3% of ω-acetyl-2-methylbenzthiazole; the bulk (85%) of the 2-methylbenzthiazole used was recovered unchanged.

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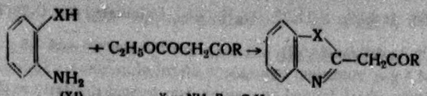
* In the work cited, the m. p. of 150° was attributed to this substance mistakenly, instead of the true value, 110-111°.

The same heterocyclic ketones, with the exception of (IV), may be prepared by other methods – the condensation of o-substituted anilines with acyl- or arylacetic esters by the scheme

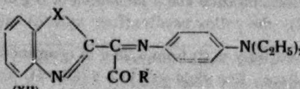


(XI) $X = NH,\ R = C_6H_5$

This scheme was described by Sexton [6] for the preparation of ω-acetyl-2-methylbenzimidazole and in a general form by Wilson [7].

In this way we prepared ω-benzoyl-2-methylbenzimidazole (XI), which was not obtained in the ester condensation; a series of other ketones of this type were also prepared for a comparison of the preparative methods.

The heterocyclic ketones synthesized had active methylene groups between the heterocyclic and the carbonyl. This activity was illustrated by condensation with aldehydes and the formation of azomethine dyes (XII)



(XII)

in an oxidative condensation with dialkyl-p-phenylenediamines. These ketones gave an intense green color with ferric chloride solution; the exceptions were ω-benzoylquinaldine, which has low activity, and the completely inactive ω-benzoyl-2-methylbenzimidazole.

EXPERIMENTAL

ω-Benzoyl-2-methylbenzithiazole (I). 7.5 g of ethyl benzoate and 7.5 g of 2-methylbenzthiazole were added to a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The mixture was heated in a flask with a small column for 4 hrs, while the azeotropic mixture of benzene and the alcohol formed was slowly distilled off. 2N acetic acid was added to the thick, orange mass formed until the precipitate dissolved completely and the benzene layer was separated, washed with 5% bicarbonate solution and dried with sodium sulfate. After removal of the solvent and unreacted starting materials at up to 104° (9 mm), the residue crystallized. The substance weighed 3.5 g (27.7%) after being washed with methanol; the yellow prisms (from methanol) had m. p. 110-111°. A mixture with the substance prepared according to the data in [5] melted at 110°.

Found %: C 71.06; H 4.43; N 5.74; S 12.64. $C_{15}H_{11}ONS$. Calculated %: C 71.11; H 4.38; N 5.53; S 12.66.

ω-Benzoyl-2-methylbenzoxazole (II) was prepared from 7.5 g of ethyl benzoate, 6.65 g of 2-methylbenzoxazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 2.5 g (21.5%); the greenish needles (from aqueous methanol) melted at 88-88.5°.

Found %: C 76.06; H 4.49; N 6.13. $C_{15}H_{11}O_2N$. Calculated %: C 75.97; H 4.67; N 5.90.

ω-Benzoyl-2-methylbenzselenazole (III) was prepared from 7.5 g of ethyl benzoate, 9.8 g of 2-methylbenzselenazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 0.79 g (5.3%); the yellow prisms (from aqueous methanol) had m. p. 186.5-187°.

Found %: C 59.73; H 3.68; N 4.59. $C_{15}H_{11}ONSe$. Calculated %: C 60.01; H 3.69; N 4.66.

ω-Benzoylquinaldine (IV) was prepared from 7.5 g of ethyl benzoate, 7.15 g of quinaldine and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 1.4 g (11.3%) the bright orange prisms (from methanol) had m. p. 114-115°.

Found %: C 82.51; H 5.46; N 5.70. $C_{17}H_{13}ON$. Calculated %: C 82.57; H 5.03; N 5.67.

ω-Benzoyl-1,2-dimethylbenzimidazole (V) was prepared from 7.5 g of ethyl benzoate, 7.3 g of 1,2-dimethylbenzimidazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 1.08 g (8.6%); the light yellow needles (from methanol) had m. p. 151-151.5°.

Found %: C 77.08; H 5.68; N 11.38. $C_{16}H_{14}ON_2$. Calculated %: C 76.78; H 5.59; N 11.11.

ω-Acetyl-2-methylbenzthiazole (VI). a) 4.4 g of ethyl acetate and 7.5 g of 2-methylbenzthiazole were added to a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The mixture was heated under reflux for 24 hrs. The precipitate, which formed on cooling, was treated similarly to (I). The yield was 0.26 g (2.7%); the light yellow prisms (from methanol) had m. p. 116-116.5°.

b) The substance was prepared similarly to (I) from 6.25 g of o-aminothiophenol and 7.8 g of ethyl acetoacetate in 70 ml of xylene. The yield was 4.43 g (46.3%); the light yellow prisms (from methane) had m. p. 116-117°; a mixture with the substance obtained by method (a) melted at 116°.

Found %: C 62.96; H 4.75; N 7.38; S 16.59. $C_{10}H_9ONS$. Calculated %: C 62.80; H 4.74; N 7.32; S 16.77.

ω-(p-Methoxybenzoyl)-2-methylbenzthiazole (VII). a) The substance was prepared from 9.0 g of ethyl p-methoxybenzoate, 7.5 g of 2-methylbenzthiazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 6.36 g (44.9%); the yellow needles (from xylene) had m. p. 114-114.5°.

b) The substance was prepared similarly to (I) from 6.25 g of o-aminothiophenol and 11.1 g of ethyl p-methoxybenzoylacetate in 70 ml of xylene. The yield was 12.4 g (87.5%); the needles (from xylene) had m. p. 114-115°; a mixture with the substance obtained by method (a) melted at 114°.

Found %: C 67.98; H 4.59; N 5.04; S 11.31. $C_{16}H_{13}O_2NS$. Calculated %: C 67.82; H 4.62; N 4.94; S 11.32.

ω-(p-Chlorobenzoyl)-2-methylbenzthiazole (VIII) was prepared from 9.23 g of ethyl p-chlorobenzoate, 7.5 g of 2-methylbenzthiazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 8.02 g (55.7%); the yellow needles (from xylene) had m. p. 141-142°.

Found %: C 62.47; H 3.58; N 4.88; S 11.06; Cl 12.56. $C_{15}H_{10}ONSCl$. Calculated %: C 62.60; H 3.49; N 4.87; S 11.14; Cl 12.32.

ω-(p-Carbethoxybenzoyl)-2-methylbenzthiazole (IX) was prepared from 11.1 g of diethyl terephthalate, 14.9 g of 2-methylbenzthiazole and a suspension of 10 g of potassium ethoxide in benzene. The yield was 12.85 g (78.9%); the yellow needles (from glacial acetic acid) had m. p. 150.5-151.5°.

Found %: C 66.24; H 4.59; N 4.65; S 10.08. M 305.81 (per Rast). $C_{18}H_{15}O_3NS$. Calculated %: C 66.44; H 4.65; N 4.35; S 9.86. M 325.37.

ω-(p-Carboxybenzoyl)-2-methylbenzthiazole. 1 g of (IX) was dissolved in 20 ml of 5% alcohol solution of sodium hydroxide in the cold. The precipitate which formed after a short time (0.93 g) was dissolved in 100 ml of water and made weakly acid with 0.5 N hydrochloric acid. The weight of the precipitate was 0.83 g (90.9%); the yellow plates (from glacial acetic acid) had m. p. 251.5-252.2°.

Found %: C 64.32; H 3.76; N 4.72; S 10.96. M 263.38 (titration with alkali). $C_{16}H_{11}O_3NS$. Calculated %: C 64.63; H 3.73; N 4.71; S 10.78. M 297.32.

ω-Terephthaloyl-bis-(2-methylbenzthiazole) (X). a) After the recrystallization of (IX) from glacial acetic acid, an insoluble precipitate remained, which weighed 0.36 g (1.68%). The yellow plates (from chlorobenzene) had m. p. 255-256°.

b) The substance was prepared from 5.0 g of o-aminothiophenol and 6.12 g of terephthaloylbisacetic ester in 70 ml of xylene. The yield was 6.65 g (77.6%); the plates (from chlorobenzene) had m. p. 255-256°; a mixture with the substance prepared by method (a) melted at 255°.

Found %: C 67.56; H 3.74; N 6.58; S 15.03. $C_{24}H_{16}O_2N_2S_2$. Calculated %: C 67.27; H 3.76; N 6.54; S 14.97.

ω-Benzoyl-2-methylbenzimidazole (XI). The substance was prepared from 5.4 g of o-phenylenediamine and 9.6 g of ethyl benzoylacetate in 100 ml of xylene. The yield was 9.65 g (81.8%); the white needles (from methanol) had m. p. 195-195.5°.

Found %: C 76.23; H 5.26; N 11.89. $C_{15}H_{12}ON_2$. Calculated %: C 76.25; H 5.24; N 11.87.

ω-(p-Nitrobenzoyl)-2-methylbenzthiazole. The substance was prepared from 2.5 g of o-aminothiophenol and 4.77 g of p-nitrobenzoylacetic ester in 100 ml of dry benzene. The yield was 0.92 g (15.4%); the yellow needles (from benzene) had m. p. 211.5-212.5°.

Found %: C 60.33; H 3.34; N 9.19; S 10.88. $C_{15}H_{10}O_3N_2S$. Calculated %: C 60.39; H 3.38; N 9.39; S 10.75.

ω-Stearoyl-2-methylbenzthiazole. The substance was prepared from 2.5 g of o-aminothiophenol and 7.1 g of stearoylacetic ester in 50 ml of xylene. The yield was 3.0 g (36.1%); the white prisms (from methanol) had m. p. 59.5-60.5°.

Found %: C 75.08; H 9.73; N 3.61; S 7.81. $C_{26}H_{41}ONS$. Calculated %: C 75.12; H 9.94; N 3.37; S 7.71.

Properties of Azomethine Dyes

Heterocyclic ketone	Yield of dye (in %)	External appearance, melting point and absorption maximum in alcohol	Nitrogen content (in %)		Formula of dye
			found	calc.	
ω-Benzoyl-2-methylbenzthiazole	69.5	Orange prisms, 236-237°, 462 mμ	10.20	10.16	$C_{25}H_{23}ON_3S$
ω-Benzoyl-2-methylbenzoxazole	45.6	Orange prisms, 197-198°, 462 mμ	10.30	10.56	$C_{25}H_{23}O_2N_3$
ω-Benzoyl-2,3-dimethylbenzimidazole	32.9	Brown prisms, 174-175° (with darkening), 445 mμ	13.81	13.65	$C_{26}H_{26}ON_4$
ω-Acetyl-2-methylbenzthiazole	69.7	Red prisms, 136-137°, 450 mμ	12.80	12.99	$C_{19}H_{17}ON_3S$
ω-(p-Methoxybenzoyl)-2-methylbenzthiazole	55.7	Orange prisms, 178-179°, 460 mμ	9.38	9.48	$C_{26}H_{25}O_2N_3S$
ω-(p-Chlorobenzoyl)-2-methylbenzthiazole	76.4	Orange prisms, 164-165°, 465 mμ	9.99	9.38	$C_{25}H_{22}ON_3SCl$
ω-(p-Carbethoxybenzoyl)-2-methylbenzthiazole	36.1	Red prisms, 214-215°, 450 mμ	8.94	8.65	$C_{28}H_{27}O_3N_3S$
ω-(p-Carboxybenzoyl)-2-methylbenzthiazole	71.4	Orange prisms, 145-146°, 462 mμ	9.42	9.19	$C_{26}H_{23}O_3N_3S$
ω-Terephthaloyl-bis(2-methylbenzthiazole)	57.7	Brown prisms, 225-226°	9.79	9.52	$C_{34}H_{28}O_2N_4S_2$

Benzal derivative of ω-benzoyl-2-methylbenzthiazole. A solution of 1.26 g of ω-benzoyl-2-methylbenzthiazole and 1.06 g of benzaldehyde in 60 ml of pyridine with 3 drops of piperidine was boiled under reflux for 2 hrs. After cooling, it was poured into 5% sulfuric acid solution (weakly acid reaction). The oily precipitate formed solidified into a yellow crystalline mass. The weight of the benzoyl derivative was 1.2 g (70.3%); the prisms (from glacial acetic acid) had m. p. 119-119.5°.

Found %: C 77.24; H 4.50; N 4.41; S 9.28. $C_{11}H_{15}ONS$. Calculated %: C 77.39; H 4.46; N 4.10; S 9.39.

Azomethine dyes (XII). A suspension of equimolecular amounts of ketone and p-nitrosodiethylaniline* in 30 ml of anhydrous alcohol with 3 drops of piperidine was boiled under reflux on a water bath for half an hour. The cooled solution deposited a precipitate of the dye, which was recrystallized from alcohol (table).

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* For the condensation with ω-acetyl-2-methylbenzthiazole, p-nitrosodimethylaniline was used.

SUMMARY

2-Methyl homologs of many nitrogen heterocyclics condense with esters, forming ketones. These ketones are formed in higher yields by condensing ortho-substituted anilines with β-ketoesters. The heterocyclic ketones obtained by these reactions possess an active methylene group.

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Received March 27, 1957

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SYNTHESIS AND REACTIONS OF SOME THIAZOLIDINE DERIVATIVES

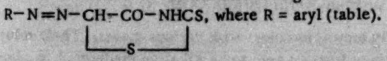
1. PREPARATION OF AZORHODANINES

A. P. Grishchuk and S. N. Baranov

Rhodanine (2-thionethiazolidone-4) is one of the most important representatives of the thiazolidines, which are especially interesting compounds in connection with the proof of the structure of penicillin, whose molecule is based on a thiazolidine ring. Rhodanine reacts readily with a series of other compounds due to its characteristically labile hydrogen atoms at position five [1].

Aldehydes [1], quinones [2], nitroso compounds [2, 3], ketones [4] and more complex oxo compounds [5] condense with rhodanine. The various rhodanine derivatives obtained by this method, have been used in a variety of ways, mainly in analytical chemistry. As Feigl [6], Kolthoff [7], Kuznetsov [8] and others have shown in their work, some rhodanines may be used as extremely sensitive reagents, which precipitate silver, mercury and copper from solutions of their salts. Starting with rhodanine, merocyanin dyes may be synthesized [9] and these are used as photosensitizers. Hydrolysis of the condensation products of aldehydes and rhodanine gives thiopyroracemic acids, which can then be readily converted to amino acids, nitriles, amines and other substances. It should be noted that the interest in rhodanines has been increasing recently as their fungicide [10, 11], goitrogenic and antithyroid properties [12] have been established and this has stimulated the study of various syntheses of rhodanine derivatives.

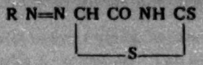
In studying the reactions of rhodanine with certain compounds, we became interested in the possibility of coupling such active materials as diazonium salts with rhodanine. It is known that the former will couple not only with amines and phenols, but also with other compounds with labile hydrogen atoms, such as for example, with pyrazolone derivatives, benzoylacetone, the anilide of acetoacetic acid, sulfazone, oxindole and others [13]. Recently diazotized sulfanilamide was successfully azo-coupled with 2-arylamino-4-thiazolidone [14]; however, there is no data in the literature on the reaction of rhodanine with diazonium salts. The syntheses we carried out in this direction gave a series of new compounds, azorhodanines, with the general formula



$R-N=N-\underbrace{CH-CO-NHCS}_{S}$, where R = aryl (table).

The substances obtained may be not only of theoretical but also of practical interest as new azo dyes. In addition, since therapeutically valuable amines were used in these syntheses, one would expect the formation of new physiologically active preparations. In this case one should take into account the fact that the introduction of a thiazolidine ring into the molecule of a substance usually results in a decrease in its toxicity [15]. Rhodanine, which has acid properties, may be compared with phenols in its role of an azo component and we therefore decided to carry out the coupling in an alkaline medium. However, rhodanine is extremely unstable in solutions of caustic alkali and even in the cold it was rapidly and completely hydrolyzed to form thioglycolic and thiocyanic acids [16]. We therefore used a weak, 3-3.5% solution of ammonia in an amount sufficient to maintain a weakly ammoniacal medium till the end of the reaction. Under these conditions at low temperature and with rapid coupling, rhodanine was hardly hydrolyzed and the bulk of the product formed was precipitated. An increase in the ammonia concentration resulted in decomposition of the diazo compound and hydrolysis and solution of the reaction product which complicated its isolation and lowered the yield. The azorhodanines which did not precipitate were isolated from the reaction solution by salting out with sodium chloride or by acidifying.

Properties of Azorhodanines with the General Formula



$R\,N{=}N\,CH\,CO\,NH\,CS$ (CH and CS joined through S)

R	Color	Melting pt. (decomp.)	Yield (in %)	Color change range (pH)	Content (in %)	
					found	calc.
C_6H_5	Yellow-orange	234—236° (decomp.)	98	10.0—11.5	N 17.75, S 26.85	N 17.71, S 27.02
p-$CH_3C_6H_4$	Orange	226—228 (decomp.)	94	7.5—11.1	N 16.65, S 25.50	N 16.71, S 25.51
$C_6H_4OCH_3$-o	Crimson	215—216 (decomp.)	95	—	N 15.90	N 15.71
$C_6H_4OCH_3$-	Brick red	188—190	97	8.8—11.4	N 15.54	N 15.71
$(CH_3)_2NC_6H_4$	Brown	125 (decomp.)	96	7.6—11.0	N 19.68	N 19.98
$(C_2H_5)_2NC_6H_4$	Brown	132—134 (decomp.)	97	8.7—11.8	N 17.56	N 18.16
$C_6H_4OC_2H_5$-p	Red-orange	207—209	91	—	N 14.84	N 14.93
C_6H_4COOH-o	Yellow	248—249 (decomp.)	91	—	N 14.89, S 22.60	N 14.93 S 22.77

The substances obtained were shown to be azo compounds by analytical determinations and by reduction which gave the original amines and breakdown products of the rhodanine ring. The materials obtained were proved to be 5-substituted rhodanines by the following: a) all the azorhodanines synthesized dissolved readily in alkalis with very intense coloring, i. e., they have acid properties while N-substituted rhodanines are neutral and insoluble in alkaline solutions; b) alkaline hydrolysis of the azorhodanines resulted in the formation of thiocyanic acid and the corresponding α-substituted thioketo acids; c) 5-substituted rhodanines, for example, 5-isopropylidenerhodanine, are incapable of combining with diazonium salts; and d) azorhodanines do not react with aldehydes.

Regarding possible isomeric forms, as our preliminary investigations showed, a hydrazone structure should be assigned to the materials obtained as this is confirmed by: a) the easy reduction of azorhodanines to amines with zinc dust in an alkaline medium; b) their solubility in concentrated sulfuric acid with intense coloring, which may be explained by weakly basic properties resulting from the imine nitrogen of the $-NH-N=$ group; c) formation by hydrolysis of hydrazothioketo acids with the structure $R\cdot NH\cdot NHCSCOOH$.

Azorhodanines are yellow, orange, red and more rarely, brown, in color with various shades. Their solutions change color very readily over a narrow pH range in going from an acid to an alkaline medium, i. e., behave as indicators. Azorhodanines are very sensitive reagents for silver, copper and mercury salts with which they form characteristically colored precipitates.

EXPERIMENTAL

5-(Phenylazo)-rhodanine (I). 4.65 g of aniline was added to a mixture of 12.5 ml of concentrated hydrochloric acid and 25 ml of water and diazotized with a solution of 3.75 g of sodium nitrite in 15 ml of water, while cooled with ice. After half an hour, a solution of 7 g of rhodanine in a mixture of 14 ml of 25% ammonia, 70 ml of water and 30 g of ice was prepared. The diazo solution was rapidly added to the solution obtained from a dropping funnel (with vigorous stirring and cooling). A yellow-orange color was immediately produced and then a suspension of a precipitate formed. After being mixed for half an hour, the reaction mixture was left for 1 hr in the cold, then the precipitated reaction product was filtered off, washed with warm dilute acid and dried. The yield was 23.2 g (98%). The crude product was dissolved in a warm 5% soda solution and precipitated with hydrochloric acid. On recrystallization from 75% alcohol, it formed right-angled yellow-orange plates with m. p. 234-236° (decomp.). It was readily soluble in methyl and ethyl alcohols, dioxane, acetone, ethyl acetate, acetic acid and aniline, difficultly soluble in ether, benzene, and xylene and insoluble in water. Solutions in alkalis had an intense red-orange color and in concentrated sulfuric acid, cherry red. A change in color from greenish yellow to pink occurred in the pH range 10.0-11.5. Aqueous alcohol solutions gave precipitates with copper, silver and mercury salts, which were brownish red, red-violet and yellow-brown, respectively in color.

Found %: N 17.75; S 26.85. $C_9H_7ON_3S_2$. Calculated %: N 17.71; S 27.02.

Reduction of (I). 0.3 g of (I) was dissolved in 15 ml of 8% NaOH and zinc dust added. Gentle heating produced complete decolorization of the solution and the simultaneous evolution of ammonia. The solution was filtered. The presence of aniline and thiocyanate ions in the solution was demonstrated by qualitative reactions.

5-(4'-Methylphenylazo)-rhodanine (II). This was prepared similarly to (I) by the diazotization of 5.4 g of p-toluidine and coupling with 7 g of rhodanine, dissolved in a mixture of 15 ml of ammonia and 80 ml of water at −2°. It formed fine orange needle-like crystals. The yield was 11.8 g (94%). It crystallized from nitrobenzene as an orange powder, decomposing at 226-228°. The product was readily soluble in most organic solvents and especially in dioxane. Solutions in alkalis were orange-red and in concentrated sulfuric acid, cherry-violet. When reduced it gave p-toluidine. A change in color from light yellow to lilac occurred in the pH range 7.5-11.1.

Found %: N 16.65; S 25.50. $C_{10}H_9ON_3S_2$. Calculated %: N 16.71; S 25.51.

5-(2'-Methoxyphenylazo)-rhodanine (III). This was formed by coupling 6.15 g of diazotized o-anisidine with 7 g of rhodanine in 110 ml of 3.5% ammonia and subsequent salting out with sodium chloride. The yield was 12.7 g (95%). The orange powder was slightly soluble in hot water and readily soluble in alcohol, dioxane, acetone and ethyl acetoacetate. From acetic acid it formed crimson red needles with m. p. 215-216° (decomp.). The substance could also be recrystallized from butanol, isoamyl alcohol and m-xylene. Alkaline solutions were bright red in color. The material dissolved in concentrated sulfuric acid to give an intense violet color, which disappeared on dilution with water.

Found %: N 15.90. $C_{10}H_9O_2N_3S_2$. Calculated %: N 15.71.

5-(4'-Methoxyphenylazo)-rhodanine (IV). This substance was prepared similarly to (III) from the diazo compound of p-anisidine and rhodanine. Salting out was not required. The yield was 13.0 g (97%). The substance formed a red powder. It was insoluble in water, readily soluble in alcohols and other organic solvents and very readily soluble in pyridine. Three reprecipitations from dioxane with water gave red-orange needles with m. p. 188-190° (decomp.). Solutions in alkalis were bright red and in concentrated sulfuric acid, violet. A change in color from light yellow to orange-pink occurred in the pH range 8.8 to 11.4.

Found %: N 15.54. $C_{10}H_9O_2N_3S_2$. Calculated %: N 15.72.

5-(4'-Dimethylaminophenylazo)-rhodanine (V). This compound was prepared similarly to (III) from 3.0 g of rhodanine in 40 ml of 3.5% ammonia and diazotized p-dimethylaminoaniline. The yield was 5.2 g (96%). The dark brown powder was soluble in acids, alkalis and the bulk of organic solvents. Solutions in chloroform, benzene, aniline and nitrobenzene, in contrast to others, had an extremely intense cherry red color. Precipitation from ethanol with water gave fine needles, decomposing at 125°. A change in color from yellow-brown to lilac occurred in the pH range from 7.6-11.0.

Found %: N 19.68. $C_{11}H_{12}ON_4S_2$. Calculated %: N 19.98.

5-(4'-Diethylaminophenylazo)-rhodanine (VI). This substance was prepared in 97% yield (15 g) by reacting diazotized p-diethylaminoaniline sulfate (12.5 g) with 7.5 g of rhodanine in 100 ml of 3.5% ammonia. Coupling was accompanied by slight foaming. The reaction mixture was kept for 12 hrs in ice and water, then the dye was filtered off and air dired. The dark red, finely crystalline powder decomposed at 131-133°. It was similar to (V) in solubility. There was a noticeable color change in the pH range 8.7-11.8.

Found %: N 17.56. $C_{13}H_{16}ON_4S_2$. Calculated %: N 18.17.

5-(4'-Ethoxyphenylazo)-rhodanine (VII). 17.4 g of p-phenetedine hydrochloride was diazotized and coupled at −5 to 0° with 15.0 g of rhodanine in 28 ml of ammonia, 80 ml of water and 50 g of ice. The diazo solution was added over a period of 20 min. After 12 hrs, the dye was filtered off and washed with water. Part of the dye precipitated from the diluted mother liquor. The total yield was 26 g (91%). The red powder, consisting of fine needles, was readily soluble in methanol and ethanol and difficultly soluble in ether, benzene and chloroform; it dissolved with heating in acetone, dioxane, xylene and ethyl acetoacetate; it was insoluble in water. It crystallized from acetic acid as red-orange needles with m. p. 207-209°. A solution in concentrated sulfuric acid was intense violet and an alkaline solution, bright red.

Found %: N 14.84. $C_{11}H_{11}O_2N_3S_2$. Calculated %: N 14.93.

5-(2'-Carboxyphenylazo)-rhodanine (VIII). 3.45 g of anthranilic acid was diazotized and coupled at 0° with 3.8 g of rhodanine in 9.5 ml of ammonia and 40 ml of water. After 2 hrs, 10 g of sodium chloride was added and after a further 1 hr, the precipitated dye was filtered off and carefully washed with cold water. The red-orange powder became deeper in color on heating. The yield was 13 g (91%). The product crystallized from 93% alcohol, acidified with hydrochloric acid, as light yellow needles, which were readily soluble in dioxane, in water and alcohol on heating and slightly soluble in ether. The m. p. was 248-249° (decomp.). The substance gave yellow precipitates with salts of iron, lead, cobalt and cadmium. The sensitivity of the reaction with silver salts made it possible to determine the solubility of metallic silver in water.

Found %: S 22.60; N 14.89. $C_{10}H_7O_3N_3S_2$. Calculated %: S 22.77; N 14.93.

SUMMARY

Synthesis conditions are proposed for compounds of diazonium salts with rhodanine which were previously unknown; 8 new substances, azorhodanines, were prepared and are described. The materials synthesized have acid properties and are 5-arylazo substituted rhodanines.

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Received April 2, 1957

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* Original Russian pagination. See C. B. translation.

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INVESTIGATION OF THE CHEMISTRY OF ORGANIC OXIDES

XIV. REACTION OF THE α-OXIDE OF ISOPRENE WITH AMMONIA AND AMINES

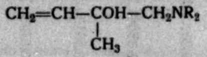
V. M. Al'bitskaia and A. A. Petrov

In a previous report we characterized the hydroxyamines formed by reacting divinyl oxide with primary and secondary amines [1]. The present paper describes the results of our experiments on the reactions of isoprene α-oxide (1,2-epoxy-2-methylbutene-3) with ammonia and amines. We could find no data on this problem in the literature.

By adding ammonia and four primary (from methyl-to butylamine) and four secondary (from dimethylamine to dibutylamine) amines to isoprene oxide, 9 amine alcohols were prepared with the constants given in the table. A comparison of the constants of these substances with those of the products obtained under similar conditions from divinyl oxide shows the considerably lower boiling points of the former, which are remarkable as these substances have an extra methyl group. The boiling points rise, the specific gravities decrease and the refractive indexes fall in the case of secondary amines and rise in the case of tertiary amines, along the homologous series of the amine alcohols prepared.

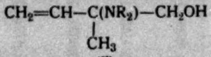
All the amino alcohols prepared form well-crystallized picrolonates. Their melting points (given in the table) decrease regularly along the homologous series.

From the addition of ammonia and amines to isoprene α-oxide, one would expect the formation in each case of two isomeric amino alcohols with a primary and a tertiary hydroxy group.



$$CH_2{=}CH{-}\underset{CH_3}{\underset{|}{C}}OH{-}CH_2NR_2$$

(I)



$$CH_2{=}CH{-}\underset{CH_3}{\underset{|}{C}}(NR_2){-}CH_2OH$$

(II)

As Krasusskii's rule for reactions of primary-tertiary oxides in alkaline reagents is closely followed [2], we assigned structure (I) to the products of ammonia and amine addition to isoprene oxide.

With the purpose of finding other possible isomers of the amino alcohols, we carried out another experiment on the addition of methylamine to isoprene oxide, using considerably greater amounts of the starting materials. Distillation of the reaction products from this experiment gave, in addition to the amino alcohol described in the table, another amino alcohol (10-12% of the mixture) with a higher boiling point.

A comparison of the infrared spectra of these isomeric amino alcohols leaves no doubt that both contain a vinyl group. The double bond gives a band at 1646 cm^{-1} in both spectra and the bands at 923-926 cm^{-1} (strong) and 990-1003 cm^{-1} (average) correspond to the CH-deformation vibrations in the vinyl group. The two substances have equal absorptions at 6100 cm^{-1} which is very characteristic of vinyl compounds [3]. Consequently, the amino alcohol with the higher boiling point could only be assigned formula (II).*

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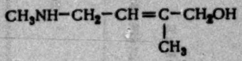
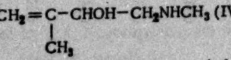
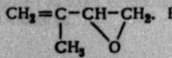
* Besides Formulas (I) and (II), the isomeric amine alcohols could have formula  $CH_3NH{-}CH_2{-}CH{=}\underset{CH_3}{\underset{|}{C}}{-}CH_2OH$ (III) (1,4-addition) or formula  $CH_2{=}\underset{CH_3}{\underset{|}{C}}{-}CHOH{-}CH_2NHCH_3$ (IV), if the initial oxide contained traces of the isomer . Both of these formulas are excluded.

TABLE 2

Constants and Data for the Obtaining of Amino Acids

Substance	Boiling point at 20 mm	d_4^{20}	n_D^{20}	MR_D		Found (%)			Calculated (%)			Picrolonates		
				found	calc.	C	H	N	C	H	N	melting point	% N found	% N calc.
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2NH_2$	75—75.5°	0.9581	1.4698	29.44	29.77	59.44	10.90	—	59.37	10.96	—	195—196°	18.73	19.17
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2NHCH_3$	59.5—60	0.9040	1.4522	34.38	34.57	62.32, 62.44	11.67, 11.52	12.38, 12.30	62.56	11.38	12.16	214—215	18.38, 18.55	18.46
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2NHC_2H_5$	70—71	0.8821	1.4509	39.43	39.19	65.36, 65.42	11.78, 12.01	11.28, 11.19	65.07	11.70	10.84	195—196	17.53, 17.83	17.81
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2NHC_3H_7$	82—83	0.8726	1.4461	43.78	43.80	66.88, 67.03	12.06, 12.07	9.86, 9.89	67.08	11.96	9.78	188—189	16.97, 17.12	17.19
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2NHC_4H_9$	97—99	0.8670	1.4470	48.46	48.42	68.48, 68.62	12.29, 12.21	9.05, 9.15	68.74	12.17	8.91	179—180	16.49, 16.34	16.62
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2N(CH_3)_2$	50.5—51.5	0.8584	1.4378	39.49	39.53	65.23, 64.97	11.88, 11.92	11.01, 10.92	65.07	11.70	10.84	136—137	17.56, 17.66	17.81
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2N(C_2H_5)_2$	75—76	0.8513	1.4394	48.62	48.76	68.82, 69.19	12.06, 12.23	9.05, 9.31	68.74	12.17	8.91	119—120	16.80, 16.69	16.62
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2N(C_3H_7)_2$	100—102	0.8483	1.4421	57.81	58.00	71.68, 71.54	12.50, 12.64	7.37, 7.48	71.30	12.51	7.56	98—99	15.95, 15.69	15.58
$CH_2{=}CH{-}\underset{\displaystyle CH_3}{\underset{\mid}{COH}}{-}CH_2N(C_4H_9)_2$	127—128	0.8470	1.4444	66.97	67.23	72.92, 73.10	12.89, 12.88	6.83, 6.73	73.18	12.75	6.57	94—95	14.67, 14.40	14.67

The same frequencies are found in the spectrum of the amino alcohol prepared from isoprene oxide and dimethylamine.

Thus,using methylamine as an example, it was shown that amines were added to isoprene oxide in two directions; however, a very small degree of addition, contrary to V. V. Markovnikov's rule, occurred.

EXPERIMENTAL

Isoprene oxide (1,2-epoxy-2-methylbutene-2) was prepared by distilling the bromohydrin over alkali and the former was obtained from isoprene by the method described previously [4]. About 150 g of oxide with b. p. 79-80°, d^{20}_4 0.8547, n^{20}D 1.4142 was used for the work.

When isoprene oxide was reacted with a 10-fold excess of 33% aqueous ammonia solution under normal conditions, the yield of monoalkenolamine was about 50%. In addition we obtained a higher fraction, which partly crystallized. It was not examined more closely.

When isoprene oxide (0.1-0.2 mole) was reacted with 3-5-fold excess of 33% aqueous solutions or emulsions of amines (the mixture of reagents was stirred for several hours and then left to stand for 1-2 days), the yields of amino alcohols varied over the range 60-75%. Analytical data for all the compounds isolated are given in the table.*

A large-scale experiment using 48 g of isoprene oxide and 170 g of methylamine yielded 52 g of a mixture of amino alcohols, which was vacuum distilled to give the amino alcohol described in the table (44 g) and an amino alcohol with the constants given below (4.5 g).

B. p. 87-89° (20 mm), d^{20}_4 0.9356, n^{20}D 1.4624. Found %: C 62.41; H 11.34; N 12.65. $C_6H_{13}ON$. Calculated %: C 62.57; H 11.38; N 12.16.

The picrolonate had m. p. 187-188°.

SUMMARY

1. The reaction of isoprene oxide with ammonia and some primary and secondary amines was investigated.

2. It was established that the reaction gave mainly unsaturated amino alcohols with a tertiary alcohol group. Using methylamine as an example, it was shown that isomeric amino alcohols with a primary alcohol group were obtained as 10-12% amounts of the mixture.

3. Ten unsaturated amino alcohols were prepared and characaterized. Crystalline picrolonates were prepared from all the substances.

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Received April 4, 1957

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* The analyses were performed by I. A. Maretina, and the authors would like to thank her for them.

** Original Russian pagination. See C. B. translation.

*** In Russian.

INVESTIGATION OF ISOMERIZATION AND DIMERIZATION OF DIMETHYLVINYLCARBINOL RELATIVE TO THE pH OF THE REAGENT

III. THE EFFECT ON DIMETHYLVINYLCARBINOL OF HYDROCHLORIC ACID, SATURATED WITH SODIUM AND MAGNESIUM CHLORIDES, AND HYDROFLUORIC ACID

A. I. Lebedeva and L. F. Almashi

The investigation of dimethylvinylcarbinol reactions in relation to the pH of the reagent was begun in previous papers [1, 2]. In the present work we decided to try the effect on dimethyvinylcarbinol of such strongly acid reagents as hydrofluoric acid and saturated solutions of sodium and magnesium chlorides in hydrochloric acid at various concentrations.

The pH was measured potentiometrically with a hydrogen electrode.

Reaction of the above reagents with dimethylvinylcarbinol gave a mixture of products from which we isolated and identified isoprene, the original dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of dimethylvinylcarbinol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, linalool and geraniol. Table 1 gives the yields of the products obtained as percents of the dimethylvinylcarbinol that reacted.

The results obtained show that with a decrease of the pH of the reagent, the amount of dimethylvinylcarbinol recovered from the reaction decreased and the yield of terpene alcohols increased.

A certain similarity may be drawn here with the data given by Komarewsky and Shih [3], who established that the polymerization of isoprene depended on the concentration of acids at room temperature. For some reason the authors did not note in their work that the yield of dimer and polymer fractions was very strongly affected by not only the concentration, but also the strength of the acid, as at equal concentrations, sulfuric acid has a much greater effect than phosphoric acid. It should be noted that with a decrease in the pH of the reagent, the yield of

TABLE 1

Expt. no.	Reagent	pH of Reagent	Isoprene	Dimethylvinylcarbinol recovered	γ,γ-Dimethylallyl alcohol	γ,γ-Dimethylallyl ether of dimethylvinylcarbinol	γ,γ-Dimethylallyl ether of γ,γ-dimethylallyl alcohol	Linalool	Geraniol
1	1-N HCl, saturated with NaCl	+0.15	6.0	34.0	12.1	9.0	2.4	Traces	Traces
2	1-N HCl, saturated with $MgCl_2$	−0.18	7.6	21.4	8.9	20.4	5.0	2.0	Traces
3	1-N HF	−0.25	10.0	20.4	7.5	22.6	8.0	3.0	Traces
4	5-N HF	−0.96	14.8	17.6	9.7	14.5	6.0	6.0	3.1
5	10-N HF	−1.43	9.0	12.0	4.5	9.0	17.0	9.0	4.5
6	10-N HCl, saturated with NaCl	−1.76	10.8	6.4	3.8	8.7	16.6	8.9	3.2
7	10-N HCl, saturated with $MgCl_2$	−1.93	12.7	6.3	2.3	10.5	14.8	10.5	4.2

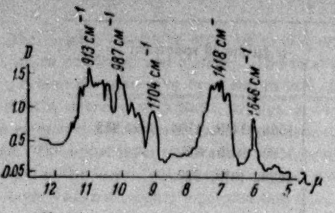

Fig. 1. Infrared spectrum of dimethylvinylcarbinol.

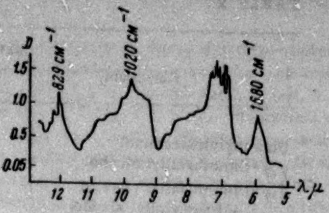

Fig. 2. Infrared spectrum of β,β-dimethylallyl alcohol.

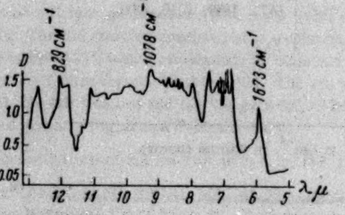

Fig. 3. Infrared spectrum of γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol.

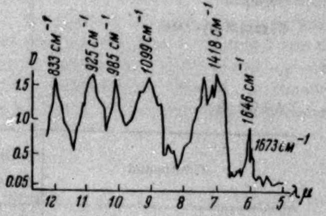

Fig. 4. Infrared spectrum of linalool (synthetic).

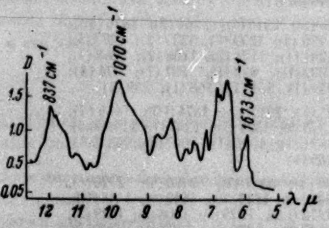

Fig. 5. Infrared spectrum of geraniol (synthetic).

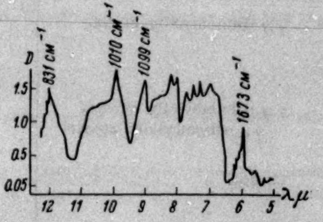

Fig. 6. Infrared spectrum of geraniol hydrate.

isoprene and unsaturated ethers increased and this indicated a considerable and, in this case, unwanted acceleration of the processes of molecular and intermolecular dehydration. Another interesting fact is that with a decrease in pH the yield of primary-tertiary ether decreased and the yield of diprimary ether increased, but the total yield of unsaturated ethers remained almost constant.

In addition to linalool and geraniol, Expts. 6 and 7 yielded a higher boiling fraction (2 and 4%, respectively) which according to elementary analysis, active hydrogen content, molecular weight determination and physical constants could be considered geraniol hydrate, first prepared by Pfauu and Plattner [4].

Most probably, the geraniol hydrate was formed in this case by geraniol hydration.

Raman (Table 3) and IR spectra were plotted for the compounds isolated (Figs. 1-6). The most characteristic data are given in Table 2.

The data obtained show that the Raman spectra of dimethylvinylcarbinol and linalool have maxima with frequencies of 1642-1643 cm^{-1}, which indicate a primary-tertiary double bond [5]. The presence of this bond is confirmed in the IR spectra by the frequencies 1646 and 1418 cm^{-1}. The Raman spectra of γ,γ-dimethylallyl

TABLE 2

Compound	$\Delta\nu$ cm^{-1} in the Raman spectrum	ν in the IR spectrum
Dimethylvinylcarbinol	1643 (10)	1646, 1418, 1104, 987, 913
γ,γ-Dimethylallyl alcohol	1676 (10)	1680, 1020, 829
γ,γ-Dimethylallyl ether of γ,γ-dimethylallyl alcohol	1674 (10)	1673, 1078, 829
Linalool	1674 (10), 1642 (8)	1673, 1646, 1418, 1099, 985, 925, 853
Geraniol	1674 (10)	1673, 1010, 837
Geraniol hydrate	—	1673, 1099, 1010, 831

TABLE 3

Compound	Boiling point (pressure in mm)	ν cm^{-1} in Raman spectra
Dimethylvinylcarbinol	96—97°	3086 (1); 3046 (4); 3008 (1); 2976 (5); 2921 (4); 2867 (2); **1643** (10); 1449 (6); 1407 (2); 1289 (6); 1231 (1); 1031 (1); 946 (5); 917 (4); 885 (2); 726 (10); 670 (0.5)
γ,γ-Dimethylallyl alcohol	49 (10)	2978 (2); 2918 (4); 2864 (2); **1676** (10); 1450 (8); 1379 (8); 1327 (2); 1297 (1); 1241 (1); 1181 (2); 1108 (2); 1068 (1); 1003 (1); 933 (1); 881 (1); 774 (4); 729 (1); 511 (1); 368 (1); 239 (1)
γ,γ-Dimethylallyl ether of γ,γ-dimethylallyl alcohol	55 (3)	2973 (1); 2919 (2); **1674** (10); 1446 (7); 1379 (5); 1327 (3); 1241 (1); 1196 (0.5); 1121 (1); 1066 (1); 1007 (2); 933 (0.5); 765 (1)
Linalool	69 (3)	3128 (3); 3047 (2); 2980 (5); 2920 (8); 2464 (5); **1674** (10); **1642** (8); 1448 (10); 1412 (1.5); 1379 (5); 1306 (2); 1229 (2); 1142 (2); 1076 (3); 1027 (1); 922 (1); 839 (1); 818 (1); 759 (2); 720 (1); 628 (1); 542 (1); 256 (2)
Geraniol	98 (3)	3041 (1); 2971 (2); 2919 (4); 2854 (2); **1674** (10); 1446 (8); 1378 (4); 1320 (1); 1077 (0.5); 1041 (0.5); 910 (0.5); 794 (0.5); 721 (1); 249 (0.5)

alcohol, γ,γ-dimethylallyl ether, linalool, geraniol and geraniol hydrate contain the frequency 1674-1676 cm^{-1}, characteristic of a secondary-tertiary double bond. The IR spectra have characteristic maxima at 1673-1680 cm^{-1}, which correspond to the C=C bond vibration of a trisubstituted ethylene bond [6] and at 829-837 cm^{-1}, which correspond to the deformation vibration of C—H at the same bond. The frequency 1078 cm^{-1}, obtained in the case of γ,γ-dimethylallyl ether, may correspond to the C—O bond vibration of ethers. The frequency 1010-1020 cm^{-1} corresponds to the vibration of the C—O bond in primary alcohols.

The IR spectral data obtained for synthetic linalool and geraniol agree within the limits of experimental error with those in the literature [6].

EXPERIMENTAL

The reagent was added dropwise to 50 g of anhydrous dimethylvinylcarbinol, placed in a three-necked flask with a reflux condenser and a stirrer. The total amount of hydrochloric and hydrofluoric acids for each experiment was kept the same. For example, in Expt. 1 we used 50 g of 1 N HCl, saturated with NaCl, in Expt. 6, 5 g of 10 N HCl, saturated with NaCl, in Expt. 3, 50 g of 1 N HF and in Expt. 5, 5 g of 10 N HF. The mixture was stirred vigorously for 96 hrs at room temperature, 3 hrs at 30-40° and 3 hrs at 70-80°. The layers were then separated. The upper layer was washed with aqueous soda solution and dried with potassium carbonate. An ether extraction of the lower layer yielded original dimethylvinylcarbinol and traces of high boiling compounds. The upper layer was first roughly separated into three fractions and then each fraction was fractionated on a column.

The 1st fraction with b. p. 34-36° was mainly isoprene. The anhydride of 5-methyltetrahydrophthalic acid had m. p. 64°. The 2nd fraction corresponded to the original dimethylvinylcarbinol in its constants. The Raman spectrum was plotted with a 7-hr exposure and a 0.07 mm slit (Table 3). The infrared absorption spectrum was plotted on a Hilger spectrometer with a slit width of 1.2-2 cm^{-1}. The thickness of the absorbing layer was 45μ (Fig. 1). The 3rd fraction consisted of γ,γ-dimethylallyl alcohol. The melting point of the acid 3-nitrophthalic ester was 128-129°, which corresponds to literature data [7]. The 4th fraction corresponded to the γ,γ-dimethylallyl ether of dimethylvinylcarbinol [2]. The 5th fraction was the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, the 6th linalool and the 7th geraniol. The geraniol was purified via its calcium chloride compound. The data are given in Fig. 5 and Tables 2 and 3.

Investigation of 8th fraction with b. p. 148-150° (10 mm).

$n^{19}D$ 1.4738, d^{19}_4 0.9484, MR_D 51.02; calculated 50.96. Found %: C 69.49; H 11.84; M 175.8; number of active hydrogens 1.96. $C_{10}H_{20}O_2$. Calculated %: C 69.72; H 11.70. M 172.3; number of active hydrogens 2.00.

2.8 g of the substance with b. p. 148-150° (10 mm) in 20 ml of chloroform was ozonized at −70°. 0.91 g of ozone was added. The ozonide (3.5 g) was decomposed with water. Traces of formaldehyde and formic acid were found. 66% of the theoretical amount of acetone was found. The IR spectrum of geraniol hydrate is given in Fig. 6 and Table 2.

SUMMARY

1. The effect of strongly acid reagents on dimethylvinylcarbinol was investigated and a definite relation of reaction product yields to pH of the reagent was found.

2. A decrease in the value of the reagents pH decreased the percent of dimethylvinylcarbinol recovered from the reaction and increased the yield of terpene fractions, i. e., a decrease in the pH of the reagent promoted dimerization and polymerization.

3. Strongly acid reagents reacted with dimethylvinylcarbinol to give, in addition to terpene alcohols, the product of their hydration — geraniol hydrate.

4. Raman spectra were plotted for dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, synthetic linalool and geraniol.

5. IR spectra were plotted for dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, synthetic linalool, geraniol and geraniol hydrate.

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Received May 21, 1957

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INVESTIGATION OF ETHERS WITH A DOUBLE BOND IN THE ALLYL POSITION

III. STUDY OF THE ETHERIFICATION OF $\alpha,\alpha,\gamma,\gamma$-TETRAALKYL SUBSTITUTED ALLYL ALCOHOLS

V. I. Pansevich-Kollada and I. F. Osipenko

In previous reports [1, 2] we showed that $\alpha,\alpha,\gamma,\gamma$-tetraalkyl substituted allyl alcohols very readily form ethers when treated with primary monoatomic alcohols of the aliphatic series in the presence of a small amount of sulfuric acid.

The present work is devoted to a study of how the etherification of tetraalkyl substituted allyl alcohols is affected by the structure of primary alcohols, the nature of the alcohol groups (primary, secondary, tertiary), the possibility of using heterofunctional compounds containing a primary alcohol group, for the etherification, and also the possibility of forming ethers of the allyl alcohols being studied with di- and triatomic alcohols.

With this in mind and using the conditions described previously [1, 2], we etherified 2,4-dimethylpenten-2-ol-4 (I), 2,4-dimethylhexen-2-ol-4 (II), 2,4-dimethylhepten-2-ol-4 (III) and 2,4-dimethylocten-2-ol-4 (IV) with various hydroxyl-containing compounds.

The reaction of alcohols (I and II) with allyl alcohols in the presence of sulfuric acid readily gave the corresponding diallyl ethers – 2,4-dimethyl-4-allyloxypentene-2 (V) and 2,4-dimethyl-4-allyloxyhexene-2 (VI).

Alcohol (IV) was readily etherified with benzyl alcohol and alcohol (II) with β-phenylethyl alchol to give 2,4-dimethyl-4-benzyloxyoctene-2 (VII) and 2,4-dimethyl-4-(β-phenylethoxy)-hexene-2 (VIII), respectively.

Etherification of alcohol (II) with heterofunctional compounds, ethylene chlorohydrin and β-ethoxyethanol, also gave ethers – 2,4-dimethyl-4-(β-chloroethoxy)-hexene-2 (IX) and 2,4-dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X), respectively.

We studied the effect of the nature of the alcohol group of the second component on the etherification of $\alpha,\alpha,\gamma,\gamma$-tetraalkyl substituted allyl alcohols using the reaction of alcohol (II) with the secondary alcohols, propanol-2 and octanol-2. No ethers were formed in either case. No ethers were obtained from these alcohols and the tertiary alcohol 2-methylbutanol-2 and phenol. Under the same conditions, alcohol (III) and cyclohexanol gave a small yield of 2,4-dimethyl-4-cyclohexoxyheptene-2 (XI).

Thus, $\alpha,\alpha,\gamma,\gamma$-tetraalkyl substituted allyl alcohols were readily etherified only with those compounds which contain a primary alcohol group.

Allyl ethers of polyhydroxy compounds have been described several times in the literature [3-10]. Some of them have the valuable capacity of forming stable, transparent and insoluble films [3, 4]. It was therefore interesting to study the etherification of $\alpha,\alpha,\gamma,\gamma$-tetraalkyl substituted allyl alcohols with di- and triatomic alcohols.

We etherified alcohols (II), (III) and (IV) with ethylene glycol and glycerol. In the case of the ethylene glycol, the reaction proceeded analogously to the etherification with primary monoatomic alcohols and gave simultaneously the corresponding mono- and diethers of ethylene glycol (XII-XVI).

The reaction products of alcohols (II)-(IV) and glycerol were glycerol diethers. As $\alpha,\alpha,\gamma,\gamma$-tetraalkyl substituted allyl alcohols did not form ethers with secondary alcohols and as there were no glycerol triethers in the reaction products, the structure of the glycerol diethers we prepared could be expressed by the formulas (XVII)-(XIX).

Characteristics of Ethers Obtained

Name of ether	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
2,4-Dimethyl-4-allyloxypentene-2 (V) $C_{10}H_{18}O$	49.5—50.5° (10)	1.4406	0.8240
2,4-Dimethyl-4-alloxyhexene-2 (VI) $C_{11}H_{20}O$	59.5—60.5 (9)	1.4431	0.8311
2,4-Dimethyl-4-(benzyloxy)-octene-2 (VII) $C_{17}H_{26}O$	132—133.5 (5—6)	1.4967	0.9174
2,4-Dimethyl-4-(β-phenylethoxy)-hexene-2 (VIII) $C_{16}H_{24}O$	132—132.5 (6)	1.4964	0.9205
2,4-Dimethyl-4-(β-chloroethoxy)-hexene-2 (IX) $C_{10}H_{19}OCl$	62—62.5 (2)	1.4522	0.9445
2,4-Dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X) $C_{12}H_{24}O_2$	95.5—96.5 (10)	1.4374	0.8661
2,4-Dimethyl-4-cyclohexoxyheptene-2 (XI) $C_{15}H_{28}O$	101 (8)	1.4582	0.8718
2,4-Dimethyl-4-(β-hydroxyethoxy)-hexene-2 (XII) $C_{10}H_{20}O_2$	68—69 (1)	1.4534	0.9220
2,4-Dimethyl-4-(β-hydroxyethoxy)-heptene-2 (XIII) $C_{11}H_{22}O_2$	86.5—88 (1.5)	1.4549	0.9104
2,4-Dimethyl-4-(β-hydroxyethoxy)-octene-2 (XIV) $C_{12}H_{24}O_2$	94.5—95 (2)	1.4550	0.9006
1,2-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-ethane (XV) $C_{18}H_{34}O_2$	112—114 (1)	1.4551	0.8814
1,2-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-ethane (XVI) $C_{22}H_{42}O_2$	161—163 (1—2)	1.4582	0.8688
1,3-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-propanol-2 (XVII) $C_{19}H_{36}O_3$	136.5—138 (1.5)	1.4646	0.9117
1,3-Di-(1,3-dimethyl-1-n-propylbuten-2-oxy)-propanol-2 (XVIII) $C_{21}H_{40}O_3$	143—144 (1)	1.4640	0.9133
1,3-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-propanol-2 (XIX) $C_{23}H_{44}O_3$	158.5—160 (1)	1.4639	0.9067
2,4-Dimethyl-4-(2,3-dihydroxypropoxy)-heptene-2 (XX) $C_{12}H_{24}O_3$	134—136 (1)	1.4661	0.9651

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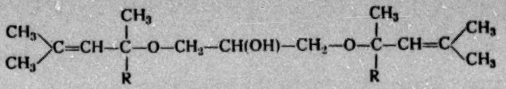
* The high molecular weight of ether (XX) is probably due to association of the molecules of

MR_D		Found (%)			Calculated (%)			M	
found	calc.	C	H	OH	C	H	OH	found	calc.
49.16	49.09	77.88	11.81	—	77.86	11.76	—	149.8, 153.0	154.24
53.65	53.70	78.34	12.36	—	78.50	12.27	—	163.9, 166.7	168.16
78.52	78.28	82.50	10.73	—	82.86	10.65	—	289.5, 242.4	246.2
73.80	73.66	82.69	10.66	—	82.70	10.41	—	—	—
54.49	54.42	—	—	—	—	—	—	187.7	190.7
60.64	60.53	72.10	12.20	—	71.95	12.08	—	189.5, 194.7	200.3
70.25	70.44	80.07	12.32	—	80.29	12.58	—	217.2, 217.5	224.2
50.54	51.08	69.66	11.72	10.00	69.72	11.70	9.87	173.2	172.26
55.52	55.70	70.90	12.14	9.49	70.92	11.91	9.12	—	—
60.35	60.38	72.20	12.35	8.12	71.95	12.08	8.49	196.3, 194.7	200.3
87.30	87.69	76.31	12.27	—	76.55	12.16	—	273.3	252.4
106.4	106.15	78.32	12.39	—	78.05	12.51	—	—	—
94.23	93.71	73.37	11.80	5.19	73.02	11.61	5.44	—	—
102.9	103.0	74.36	12.06	4.52	74.07	11.84	4.99	335.1	340.5
112.3	112.28	75.28	12.07	4.92	74.95	12.03	4.61	360.0, 354.4	368.6
62.02	61.84	67.01	11.15	15.45	66.62	11.19	15.72	241.2*, 244.2	216.3

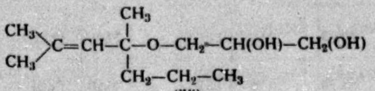
this substance, which contains two OH groups.



$$(CH_3)_2C{=}CH{-}C(CH_3)(R){-}O{-}CH_2{-}CH(OH){-}CH_2{-}O{-}C(CH_3)(R){-}CH{=}C(CH_3)_2$$

(XVII) R = C_2H_5; (XVIII) R = n-C_3H_7; (XIX) R = n-C_4H_9

A glycerol monoether (XX) was also isolated in the case of alcohol (III).



$$(CH_3)_2C{=}CH{-}C(CH_3)(CH_2{-}CH_2{-}CH_3){-}O{-}CH_2{-}CH(OH){-}CH_2(OH)$$

(XX)

The effect of the size of the hydrocarbon radical of the primary monoatomic alcohol on the reaction rate was studied using as an example the etherification of alcohol (IV) with a mixture of equimolecular amounts of methyl and n-butyl alcohols. Under these conditions the ether yield for methyl alcohol was twice as great as for n-butyl. Consequently, the rate of etherification of alcohol (IV) with methyl alcohol was relatively higher than that with n-butyl.

EXPERIMENTAL

The tertiary alcohols (I-IV) were synthesized by the Grignard reaction from mesityl oxide and the appropriate alkylmagnesium halides [11, 12].

The ethers of α, α, γ, γ-tetraalkyl substituted allyl alcohols were prepared by the procedure described in the previous report [2], except that in the case of the glycerol ethers of alcohols (II-IV), stirring was replaced by shaking the reaction mixture for 4 hrs. All the ethers prepared were colorless liquids. They dissolved readily in organic solvents, but were insoluble in water and decolorized a 1% potassium permanganate solution. Their physical constants are given in the table.

2,4-Dimethyl-4-allyloxypentene-2 (V). To 275 g (2.41 moles) of 2,4-dimethylpenten-2-ol-4 (I) was added 250 g (4.3 moles) of allyl alcohol, containing 10 ml of sulfuric acid solution. We obtained 209 g (56.2%) of ether.

2,4-Dimethyl-4-allyloxyhexene-2 (VI) was prepared from 10 g of 2,4-dimethylhexen-2-ol-4 (II) (0.078 mole) and 9.8 g (0.169 mole) of allyl alcohol, containing 0.5 ml of sulfuric acid solution. The yield was 6.8 g (53.8%) of ether.

2,4-Dimethyl-4-(β-phenylethoxy)-hexene-2 (VIII). 10 g (0.082 mole) of β-phenylethyl alcohols, containing 0.2 ml of sulfuric acid solution was added to 5 g (0.039 mole) of 2,4-dimethylhexen-2-ol-4 (II). We obtained 4.53 g (44.8%) of ether as a colorless liquid with an almond smell.

2,4-Dimethyl-4-(β-chloroethoxy)-hexene-2 (IX). 14.2 g (0.175 mole) of 2-chloroethanol, containing 0.5 ml of sulfuric acid solution, was added to 10 g (0.078 mole) of alcohol (II). We obtained 7.34 g (49.3%) of ether as a colorless mobile liquid with a slightly irritating smell.

Found %: Cl 18.11. $C_{10}H_{19}OCl$. Calculated %: Cl 18.59.

2,4-Dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X) was prepared from 10.2 g (0.079 mole) of alcohol (II) and 18.69 g (0.23 mole) of 2-ethoxyethanol, containing 1 ml of sulfuric acid solution. The yield of ether was 8.16 g (50.4%).

2,4-Dimethyl-4-(β-hydroxyethoxy)-hexene-2 (XII) was prepared from 10.2 g (0.079 mole) of alcohol (II) and 20.2 g (0.358 mole) of ethylene glycol, containing 1.2 ml of sulfuric acid solution. The product was an immobile, colorless liquid. The yield of the glycol monoether was 4.57 g (33.2%).

1,2-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-ethane (XV). 1.95 g (17.3%) of this substance was obtained at the same time as the glycol monoether (XII). It was a colorless, oily liquid.

1,3-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-propanol-2 (XVII). 30 g (0.326 mole) of glycerol, containing 2 ml of aqueous sulfuric acid solution, was added to 15 g (0.117 mole) of alcohol (II). We obtained 4.02 g (21.9%) of the diether of glycerol as a colorless, immobile liquid.

2,4-Dimethyl-4-cyclohexoxyheptene-2 (XI) was prepared from 10 g (0.07 mole) of 2,4-dimethylhepten-2-ol-4 (III) and 14 g (0.14 mole) of cyclohexanol, containing 1 ml of sulfuric acid solution. It was a clear, colorless liquid. The yield of ether was 0.57 g (3.6%).

2,4-Dimethyl-4-(β-hydroxyethoxy)-heptene-2 (XIII). 22.2 g (0.358 mole) of ethylene glycol, containing 1 ml of sulfuric acid solution, was added to 15 g (0.105 mole) of alcohol (III); a colorless immobile liquid was formed. The yield of ether was 6.9 g (55.5%).

2,4-Dimethyl-4-(2,3-dihydroxypropoxy)-heptene-2 (XX) was prepared from 15 g (0.105 mole) of alcohol (III) and 25.2 g (0.247 mole) of glycerol,containing 1 ml of aqueous sulfuric acid solution. We obtained a colorless, viscous liquid, which represented a 1.7 g (8.2%) yield of the monoether.

1,3-Di-(1,3-dimethyl-1-n-propylbuten-2-oxy)-propanol-2 (XVIII). This colorless, viscous substance was obtained at the same time as (XX) in 18.9% yield.

2,4-Dimethyl-4-(benzyloxy)-octene-2 (VII). 160 g (1.48 mole) of benzyl alcohol, containing 2.5 ml of sulfuric acid solution, was added to 120 g (0.755 mole) of 2,4-dimethylocten-2-ol-4 (IV). We obtained 120.8 g (63.4%) of the ether. The colorless, oily liquid had an ethereal smell, slightly reminiscent of the smell of benzyl alcohol.

2,4-Dimethyl-4-(β-hydroxyethoxy)-octene-2 (XIV) was obtained from 23.4 g (0.15 mole) of alcohol (IV), 18.6 g (0.3 mole) of ethylene glycol and 0.5 ml of sulfuric acid solution. The yield of the glycol monoether was 9.77 g (32%).

1,2-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-ethane (XVI). The colorless immobile liquid was obtained at the same time as the monoether (XIV) in 13% yield.

1,3-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-propanol-2- (XIX) was obtained from 29.4 g (0.15 mole) of alcohol (IV), 27.6 g (0.3 mole) of glycerol and 1.5 ml of sulfuric acid solution. We obtained a colorless, immobile liquid (3.5 g, 12.7%), which was the ether.

Etherification of 2,4-dimethylocten-2-ol-4 (IV) with a mixture of methyl and n-butyl alcohols. 15.6 g (0.1 mole) of alcohol (IV) was placed in a round-bottomed flask, fitted with a mechanical stirrer and a thermometer. With vigorous stirring, a mixture of 3.2 g (0.1 mole) of methyl alcohol, 7.4 g (0.1 mole) of n-butyl alcohol and 1 ml of aqueous sulfuric acid (1 : 5) was added in one portion. After 2.5 min, the reaction mixture, which was originally homogeneous and clear, instantaneously became turbid and its temperature rose from 16.3 to 21.4°. Stirring was continued for 30 min. Then the reaction mixture was treated by the method described previously [2] and vacuum distilled. We obtained two ethers – 2,4-dimethyl-4-methoxyoctene-2 (6.75 g, 39.6%) with b. p. 72.5-75° (10 mm), $n^{20}D$ 1.4371, d^{20}_4 0.8231 and 2,4-dimethyl-4-n-butoxyoctene-2 (4.05 g, 19.07%) with b. p. 104-105° (10 mm), $n^{20}D$ 1.4396, d^{20}_4 0.8219. We described both of these ethers in a previous report [2].

SUMMARY

1. The etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols with alcohols of various structures was studied.

2. It was established that the etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols proceeds only with compounds containing a primary alcohol group.

3. The rate of the etherification depends on the size of the hydrocarbon radical in the primary alcohol.

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Received April 15, 1957

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INVESTIGATION OF OXIDO COMPOUNDS

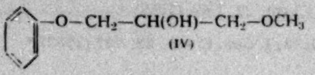
XI. REACTION OF α-OXIDES OF ALLYL ETHERS OF PHENOL, p-CRESOL AND GUAIACOL WITH METHYL ALCOHOL

V. I. Pansevich-Koliada and Z. B. Idel'chik

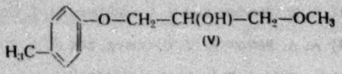
As is known, α-oxides react readily with alcohols and other oxide compounds in the presence of catalysts. This reaction was first applied by N. A. Prilezhaev [1] to 2-methylpropene-1 oxide and has since been studied many times using other α-oxides with various hydroxyl-containing compounds and catalysts [2-19]. The products of α-oxide reactions with alcohols are usually partial ethers of α-glycols. The structure of these ethers was determined by the order of opening of the oxide ring, which in its turn depended on the structure of the α-oxides and the nature of the catalyst used.

In the present work we studied the reaction of α-oxides of allyl ethers of phenol (I), p-cresol (II) and guaiacol (III) with methyl alcohol in the presence of sodium methylate.

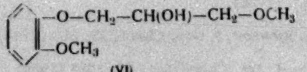
The α-oxides (I, II, III) were reacted with methyl alcohol, in which metallic sodium was first dissolved, by heating in sealed glass ampoules in a tubular furnace. We established the presence of mixed partial ethers of glycerol in the reaction products. As was shown using a series of α-oxides, in the presence of catalysts of an alkaline character, the three-membered oxide ring opens at the bond of the oxide oxygen with the more hydrogenated carbon atom and, therefore, the glycerol ethers we obtained most probably have the following structures: 1-methoxy-3-phenoxy-propanol-2 (IV), 1-methoxy-3-(p-tolyloxy)-propanol-2 (V) and 1-methoxy-3-(o-methoxyphenoxy)-propanol-2 (VI). Such structures are more probable from the point of view of steric hindrance.



(IV)



(V)



(VI)

EXPERIMENTAL

1. Preparation of 1-methoxy-3-phenoxypropanol-2 (IV). 5.5 g of the oxide of allyl phenyl ether (I) [20] was placed in a glass ampoule with 12 ml of methyl alcohol, in which 1 g of metallic sodium had been dissolved, A green ring formed at the boundary of the liquids and after shaking, the whole liquid acquired a brown color. After being heated in the sealed ampoule for 1.5 hrs on a water bath, the liquids had not mixed. After being heated at 100° for 6 hrs in a tubular furnace, the reacting mixture did not separate into layers . No pressure was found on opening the tube. The contents of the tube were poured into water. The yellowish oil which separated was extracted with ether, dried with $MgSO_4$ and vacuum distilled after removal of the ether. We obtained 3.4 g of a colorless, oily liquid with a sharp, tobacoo-like smell.

B. p. 134° (7 mm), $n^{20}D$ 1.5168, d^{20}_4 1.1130, MR_D 49.46; calculated 49.59. Found %: C 65.38; H 7.84; OH 8.28. M 183.4. $C_{10}H_{14}O_3$. Calculated %: C 65.93; H 7.69; OH 9.10. M 182.

2. Preparation of 1-methoxy-3-(p-tolyloxy)-propanol-2 (V). 2.7 g of the α-oxide of allyl p-cresyl ether (II) [21] and 5 ml of methanol, in which 0.25 g of metallic sodium had been dissolved, were heated in a glass ampoule in a tubular furnace for 3 hrs at 95°. The reaction products were treated as in the previous experiment. Distillation of the reaction products gave 0.6 g of a thick, colorless liquid with an ethereal smell.

B. p. 122° (2 mm), $n^{20}D$ 1.5135, d^{20}_4 1.0805, MR_D 54.37; calculated 54.21. Found %: C 67.96; H 8.86; OH 8.66. M 196.1. $C_{11}H_{16}O_3$. Calculated %: C 67.35; H 8.16; OH 8.67. M 196.0.

3. Preparation of 1-methoxy-3-(o-methoxyphenoxy)-propanol-2 (VI). 1.8 g of the α-oxide of the allyl ether of guaiacol (III) [21] and 3.5 ml of methanol, in which 0.25 g of metallic sodium had been dissolved, were heated in a glass ampoule in a tubular furnace for 5 hrs at 100°. The reaction products were then treated as in the previous experiments. Vacuum distillation of the reaction products yielded 0.5 g of a colorless, oily liquid, which had the smell of tobacco tar.

B. p. 155° (5 mm), $n^{20}D$ 1.5233, d^{27}_4 1.1439, MR_D 56.65; calculated 55.85. Found %: C 62.97; H 7.57; OH 7.52. M 220.8, 223.0. $C_{11}H_{16}O_4$. Calculated %: C 62.26; H 7.55; OH 8.00. M 212.0

SUMMARY

1. α-Oxides of allyl ethers of phenol, p-cresol and guaiacol were reacted with methyl alcohol in the presence of sodium methylate.

2. Three mixed partial ethers of glycerol (1-methoxy-3-phenoxy-propanol-2, 1-methoxy-3-(p-tolyloxy)-propanol-2 and 1-methoxy-3-(o-methoxyphenoxy)-propanol-2) were prepared.

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Received March 28, 1957

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THE ABNORMAL PRODUCTS OF VINYL-1-CYCLOHEXENE-3 OZONOLYSIS

A. I. Iakubchik, A. I. Spasskova, and B. I. Tikhomirov

It was noted long ago that ozonolysis products may contain materials whose formation could not be explained on the basis of the usual scheme of ozonide formation and decomposition. These materials were then called abnormal ozonolysis products. Further work and improved analysis methods showed that the formation of abnormal products in ozonolysis is a very widespread phenomenon [1, 2]. During the abnormal course of ozonization or decomposition of an ozonide, the following may occur:

1) The formation of two types of ozonides — monomer and polymer, with the formation of polymer ozonide considered as the abnormal reaction [3, 4].

2) The transfer of the double bond during ozonization [5].

3) The formation of ozonides of α-hydroperoxides, when the ozone is not only added to the double bond but also acts as a catalyst for oxidation by oxygen [2, 6].

4) The oxidizing effect of ozone [7].

5) A formate-peroxide rearrangement; Ziegler [2] found some experimental justification for this. The class of materials in which a tertiary carbon atom is in a position α to the double bond, are extremely susceptible to extraneous effects. Ziegler explained this by the lability of the bond between the tertiary carbon atom and the carbon atom at the double bond [8].

6) A change in the aldehyde intermediate reaction products. Ziegler established that on treating α-amylcaproaldehyde with acetyl hydroperoxide only 28% of α-amylcaproic acid and 48% of volatile neutral materials were obtained [2].

7) The decomposition of acids, formed by oxidative decomposition of ozonides when treated with oxidants, for example, acetyl hydroperoxide [9]. There are indications that levulinic acid undergoes changes under the effect of oxidants and light [10].

The problem of the character and extent of the course of an abnormal reaction cannot be solved simply even for substances with well-known structures. In the case of high polymers, in particular caoutchoucs, the problem is much more complicated. Some information on the possible directions of abnormal reactions may be obtained by studying the behavior of a model substance, whose structure is known and at the same time has structural characteristics similar to those of caoutchouc. Vinyl-1-cyclohexene-3 may act as a model for divinyl caoutchouc. The former is composed of two divinyl molecules, connected in positions 1,2 and 1,4. The double bond in the ring corresponds to the inner double bond and the ethylene of the vinyl group to the outer double bond of the divinyl caoutchouc macromolecules.* Other characteristics in common are a methylene group in a position α to the double bond and a labile bond between the tertiary carbon atom and the carbon atom at the double bond.

Marvel [11] found 1,2,3-propanetricarboxylic acid in the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide with hydrogen peroxide. He explained the formation of this acid by oxidative ozonolysis

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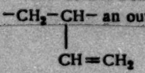
* The double bond in the unit $-CH_2-CH=CH-CH_2-$ is called an inner and the double bond in the unit



$$\begin{array}{l}-CH_2-CH-\\ \quad\ \ |\\ \quad CH=CH_2\end{array}$$

an outer bond.

of the α-methylene group. Ziegler [2] decomposed this ozonide with acetyl hydroperoxide. He found levulinic and succinic acids among the decomposition products. He explained their formation by a formate-peroxide rearrangement. On oxidizing vinyl-1-cyclohexene-3 with potassium permanganate, he found no levulinic acid, but an amount of succinic acid which was high in comparison with that obtained in the oxidative decomposition of the ozonide with acetyl hydroperoxide.

The purpose of our work was to study the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide with acetyl hydroperoxide under the conditions used in our laboratory for the ozonolysis of divinyl caoutchoucs and to examine the effect of the α-methylene group and tertiary carbon atom, connected to the vinyl group, on the formation of abnormal ozonolysis products. The acids obtained by ozonide decomposition were separated by partition chromatography.

EXPERIMENTAL

The thermopolymerization was carried out with divinyl, regenerated with zinc in an aqueous alcohol solution from divinyl tetrabromide with m. p. 116-117°. The dimer formed in the polymerization was distilled on a column of 30 theoretical plates efficiency to yield vinyl-1-cyclohexene-3.

B. p. 66.5° (100 mm), d^{20}_4 0.8310, $n^{20}D$ 1.4642, MR 36.14; calculated 36.01.

The Raman spectrum was plotted on an ISP-51 spectrograph with a 0.07 mm slit and a 6-hr exposure:

236 (1), 277 (3), 316 (1), 354 (1), 379 (2), 413 (2), 481 (1), 512 (1), 665 (2), 727 (1), 805 (3), 869 (4), 920 (3), 964 (2), 1040 (1), 1078 (2), 1140 (1), 1191 (2), 1222 (1), 1251 (3), 1292 (6), 1332 (1), 1432 (7), 1641 (9), 1650 (10), 2837 (3), 2877 (2), 2918 (8), 2997 (3), 3023 (4), 3080 (2).

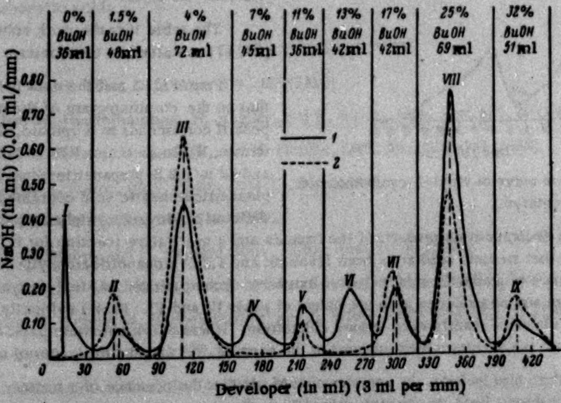


Fig. 1. Chromatograms. 1) Products of vinyl-1-cyclohexene-3 ozonolysis, 2) mixture of acids for identification of products of vinyl-1-cyclohexene-3 ozonolysis. The significance of the peaks is given in the text.

The line intensities given in brackets were evaluated visually relative to a scale of ten. The characteristics listed agree well with the data of other authors [11-14].

10 g of vinyl-1-cyclohexene-3 in ethyl acetate (b. p. 77-77.5°) was ozonized at −50°. Oxygen with a 5-6% ozone content was used for the ozonization. At the end of the ozonization, the solvent was distilled off at 15 mm and 20° until the ozonide had constant weight. Oxidative decomposition of the ozonide was performed with acetyl hydroperoxide in glacial acetic acid. Sufficient acetyl hydroperoxide was added to the ozonide solution to give 1 atom of active oxygen for each double bond. After 3 days, a two-fold amount of hydroperoxide was added and the solution was then left for a long time at room temperature. The excess hydroperoxide was decomposed with platinum black, prepared by Willstatter's method [15]. The acetic acid was distilled off at 1 mm and 30°. The products obtained formed a light yellow, viscous mass. For chromatographic analysis of the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide, a column of 15 mm diameter was loaded with 13 g of MSK [3] grade silica gel, ground up with 9 ml of water. The height of the silica gel in the column was 140 mm. Water was the stationary solvent and water-saturated butanol−chloroform mixture the mobile one. The mobile solvent was passed through the column at 1 ml a minute. The solvent coming out of the column containing the acids was collected in 3 ml portions and titrated against 0.014 N sodium hydroxide in methyl alcohol. An alcohol solution of phenolphthalein was used as the indicator. The products of oxidative decomposition were put onto the column as a tertiary amyl alcohol (b. p. 100-100.5°) solution.

Peak Volume of Acids Investigated and Artificial Mixture, Made Up for Characterizing the Products Studied

Mixture separated	Peak volume (in ml): Peak II − propionic acid	Peak III − acetic acid	Peak V − formic acid	Peak VII − succinic acid	Peak VIII − 1,2,4-butanetricarboxylic acid	Peak IX − 1,2,3-propanetricarboxylic acid
Artificial	54	114	216	297	348	408
Investigated	57	114	216	300	348	408

Figure 1 shows chromatograms of the mixture investigated and a mixture of propionic, acetic, succinic, 1,2,4-butanetricarboxylic and 1,2,3-propanetricarboxylic acids.

The table lists the peak volumes of the acids [16, 17] contained in the mixtures given above.

From Fig. 1 and the data in the table it follows that on the chromatogram of the mixture investigated, peak II corresponds to propionic, III to acetic, V to formic, VII to succinic, VIII to 1,2,4-butanetricarboxylic and IX to 1,2,3-propanetricarboxylic acids. The 1,2,4-butanetricarboxylic acid contained 3% of the carbon skeleton of vinyl-1-cyclohexene-3. Levulinic acid was not found among the decomposition products of the ozonide and a qualitative reaction for it [18] gave a negative result. It is possible that succinic acid arose from levulinic and 1,2,3-propanetricarboxylic from butanetricarboxylic acids. The presence of propionic acid indicated extensive decomposition of vinyl-1-cyclohexene-3 during the ozonolysis. There was no evidence as to the nature of peaks IV and VI. Peak I evidently consisted of a mixture of acids, which dissolved readily even in pure chloroform. It was shown chromatographically that the acetic acid, distilled off from the decomposition products of the ozonide, did not contain traces of other acids.

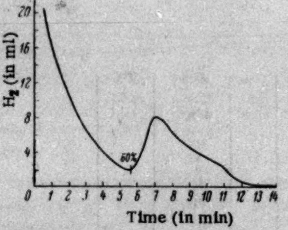


Fig. 2. Hydrogenation curve of vinyl-1-cyclohexene-3 with a Pd on $CaCo_3$ catalyst.

Since our problem also includes the consideration of whether the presence of a tertiary carbon atom connected to a carbon at the double bond, in the molecule, affects the abnormal reactions caused by the α-methylene group, we examined the behavior of ethyl-1-cyclohexene-3 during ozonolysis. Ethyl-1-cyclohexene-3 was prepared by selective hydrogenation of vinyl-1-cyclohexene-3 over a Pd on $CaCO_3$ catalyst. From the work of S. V. Lebedev and his co-workers [12, 19, 20], we expected that the vinyl group double bond would be hydrogenated much more rapidly than the double bond in the ring. The hydrogenation was carried out in a Lebedev apparatus and hydrogenation curves plotted by his method also [20]. A 0.30-0.35 g sample of vinyl-1-cyclohexene-3 was hydrogenated in ethyl alcohol in the presence of 0.1 g of catalyst. A hydrogenation curve obtained in one of these experiments is shown in Fig. 2.

By hydrogenating two samples of the substance on one catalyst, we found that the fall in the rate of hydrogenation, corresponding to the second arm of the curve, was due to a difference in the character of the bonds hydrogenated and not to exhaustion of the catalyst. In accordance with the above, vinyl-1-cyclohexene-3 was 60% hydrogenated. This should have given 80% of ethyl-1-cyclohexene-3 and 20% of ethylcyclohexane. Since for our purposes it was important that vinyl-1-cyclohexene-3 should be absent from the hydrogenation products but a trace of ethylcyclohexane would not interfere, it was decided to carry out the ozonization of ethyl-1-cyclohexene-3 in the presence of ethylcyclohexane. The hydrogenation products were treated with a saturated solution of calcium chloride several times to extract alcohol, dried over fused calcium chloride and sodium wire and distilled through a Vigreaux fractionating column, 15 cm high, at 69° and 100 mm pressure in an atmosphere of nitrogen. The product obtained had $n^{20}D$ 1.4463. According to the data in [12], the product of adding 50% hydrogen to vinyl-1-cyclohexene-3 has $n^{20}D$ 1.44847 and ethylcyclohexane $n^{20}D$ 1.43190. Ozonization, decomposition of the ozonide and separation of the ozonolysis products were performed under the conditions described above.

If the α-methylene group of the ethyl-1-cyclohexene-3 participated in the abnormal reactions, we would find β-ethylglutaric acid in the ozonolysis products. We synthesized this by Komnenos' method [21] for the chromatographic demonstration. β-Ethylglutaric acid was found in the ozonolysis products, which did not contain succinic, 1,2,4-butanetricarboxylic, 1,2,3-propanetricarboxylic and propionic acids, which must, therefore, only arise from substances containing labile 1,2 groupings.

SUMMARY

1. In addition to the normal products of vinyl-1-cyclohexene-3 ozonolysis (1,2,4-butanetricarboxylic and formic acids), abnormal products were found: succinic, 1,2,3-propanetricarboxylic and propionic acids.

2. An abnormal product, β-ethylglutaric acid, was found among the ozonolysis products of ethyl-1-cyclohexene-3.

3. The abnormal products are caused by the presence both of an α-methylene group and of a labile bond between the tertiary carbon atom and a carbon atom at the double bond.

4. In the ozonolysis products of divinyl caoutchoucs, whose macromolecules have the structural units 1,4, 1,2, 1,4, one would expect to find a low yield of 1,2,4-butanetricarboxylic and a high yield of succinic and 1,2,3-propanetricarboxylic acids.

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Received April 12, 1957

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SYNTHESIS OF ACETIC ESTER OF BIS(HYDROXYCYCLOHEXYL)-1,3-BUTADIYNE AND ITS CATALYTIC HYDROGENATION

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In a previous paper [1] we described the synthesis of the acetic ester of 2,7-dimethyl-3,5-octadiyne-2,7-diol. In the hydrogenation of this ester it was established that in the presence of platinum black or colloidal palladium the addition of 8 atoms of hydrogen yields the acetate of the saturated alcohol and the diacetate of the saturated glycol, in which connection the diacetylenic ester is capable of adding a total of 5 moles of hydrogen to yield only the acetate of the saturated alcohol.

In this paper we decide to synthesize by the same method, but at a lower temperature, the acetic ester of bis(hydroxycyclohexyl)-1,3-butadiyne and study its catalytic hydrogenation. The latter was run in the presence of either colloidal palladium or platinum black. If when the hydrogenation is run in the presence of colloidal palladium the reaction is stopped after the addition of 8 atoms of hydrogen, then after suitable treatment of the hydrogenation product a clear mobile liquid of aromatic odor is obtained, the fractionation of which gave three substances: (I) – 1,4-dicyclohexylbutane, (II) – acetate of 1-hydroxycyclohexyl-4-cyclohexylbutane, and (III) – diacetate of 1,4-bis(1-hydroxycyclohexyl)butane. Small amounts of the starting diacetylenic ester and acetic acid were also isolated.

In the presence of platinum black the diacetylenic ester is capable of adding a total of 12 atoms of hydrogen, with a gradual reduction in the reaction rate, to yield only the saturated hydrocarbon (I). In the presence of colloidal palladium the diacetylenic ester absorbs about 75% of the theoretical amount of hydrogen in the first 10 min, while in the case of platinum black this phenomenon is not observed.

Consequently, it appears that a diacetylenic ester with cyclic radicals, in contrast to esters with aliphatic radicals, yields, in addition to the acetate of the saturated alcohol and the diacetate of the saturated glycol, the saturated hydrocarbon.

EXPERIMENTAL

Synthesis of bis(1-hydroxycyclohexyl)-1,3-butadiyne diacetate. A mixture of 20 g of the glycol with m. p. 173-174°, 100 g of acetic anhydride and 1 g of anhydrous sodium acetate was heated for 1 hr in an oil bath in a flask with reflux condenser at 165-170°; further treatment was the same as described before [1].

The yield of crystals with m. p. 86-87° (from alcohol) was 21 g (78%).

Found %: C 72.54, 72.60; H 8.42, 8.31; $2CH_3CO$ 26.11, 26.75. M 329, 333 (per Rast). $C_{20}H_{26}O_4$. Calculated %: C 72.72; H 7.88; $2CH_3CO$ 26.09. M 330.

The test for active hydrogen by the Chugaev-Tserevitinov method was negative. Saponification of the ester gave the original glycol.

Hydrogenation of bis(1-hydroxycyclohexyl)-1,3-butadiyne diacetate. For hydrogenation we took 3.30 g of the ester in 50 ml of ethyl alcohol. The colloidal palladium was prepared the same as before [1]. The hydrogenation results are given in the table.

After suitable treatment the product of hydrogenation over Pd was vacuum-distilled. Here the following substances were isolated: b. p. 126-128° (4-5 mm), 0.5 g (7.57%) (I); b. p. 148-150° (4-5 mm), 1.8 g (21.41%) (II) and b. p. 73-74°, 1.5 g (14.78%) (III).

Expt. nos.	Catalyst	Weight of catalyst (in mg)	Amount of hydrogen (in ml)		
			calc.	found	amount absorbed every 5 min
1	Colloidal Pd	5	1072 ($4H_2$)	1072	475, 325, 50, 25, 20, 15, 10, 10, 14.8, 12, 6; the remaining 102 ml required 2 hrs. A total of 1072 ml was absorbed in 3 hrs
2	Pt black	1000	1460 ($6H_2$)	1435	80, 60, 50, 35, 50, 40, 50, 35, 40, 45, 40; the remaining 893 ml required 3 hrs 10 min. A total of 1435 ml was absorbed in 4 hrs 10 min

Some of the original diacetylenic ester with m. p. 86-87° and some acetic acid was also isolated.

We ran a total of 3 parallel experiments, giving similar results.

After suitable treatment of the product of hydrogenation over Pt, we isolated 3 g of (I) with b. p. 126-128° (4-5 mm), and also 1.36 g of acetic acid, from the remaining liquid.

Here we ran a total of 2 parallel experiments, giving similar results.

Analysis of Substance (I) with B. p. 126-128° (4-5 mm)

d^{20}_4 0.8853, $n^{20}D$ 1.4840, MR_D 72.13; calculated 71.69. Found %: C 85.78, 87.27; H 13.29, 14.02. M 213, 218 (cryoscopic). $C_{16}H_{30}$. Calculated %: C 86.48; H 13.51. M 222.

The tests for both active hydrogen and triple bond were negative. The substance does not decolorize potassium permanganate solution.

Analysis of Substance with B. p. 148-150° (4-5 mm) (II)

d^{20}_4 0.9548, $n^{20}D$ 1.4750, MR_D 82.63; calculated 82.58. Found %: C 76.98; H 11.86; CH_3CO 15.35. M 275 (cryoscopic). $C_{18}H_{32}O_2$. Calculated %: C 77.14; H 11.42; CH_3CO 15.35. M 280.

Analysis of Substance with M. p. 73-74°

Found %: C 70.92, 71.15; H 10.88, 10.34; $2CH_3CO$ 25.68. M 325 (cryoscopic). $C_{20}H_{34}O_4$. Calculated %: C 71.00; H 10.06; $2CH_3CO$ 25.44. M 338.

SUMMARY

1. The acetic ester of bis(hydroxycyclohexyl)-1,3-butadiyne was synthesized and described for the first time, and its catalytic hydrogenation was studied.

It was shown that in the presence of colloidal palladium the addition of 8 atoms of hydrogen yields the hydrocarbon, the acetate of the saturated alcohol and the diacetate of the saturated glycol.

In the presence of platinum black the ester is capable of adding a total of 6 moles of hydrogen to yield the hydrocarbon.

2. The compounds 1,4-dicyclohexylbutane, 1-acetoxycyclohexyl-4-cyclohexylbutane and 1,4-bis(1-acetoxycyclohexyl)butane were isolated and described in this study.

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Received June 17, 1957

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ETHERS OF GLYCOLS AND THEIR DERIVATIVES

XXXII. SYNTHESIS OF MONOETHERS OF γ-GLYCOLS AND THEIR ALKOXYMETHYL DERIVATIVES

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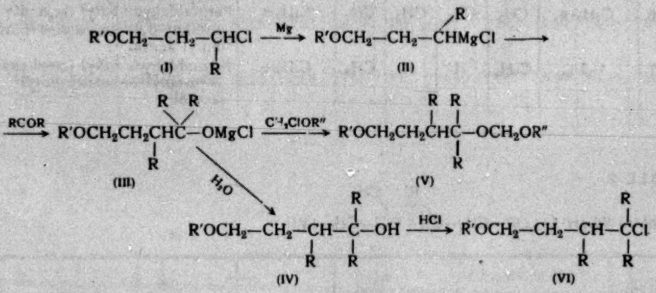
In a previous communication [1] we described the synthesis of a large number of γ-halo ethers (I), obtained by the alkylation of α-halo ethers with ethylenic hydrocarbons.

As a further aspect of studying the chemical transformations of γ-halo ethers (I), our purpose in the present study was to synthesize some 1,4-glycol monoethers (IV), some δ-alkoxy derivatives of the methylene glycol ethers (V), and some δ-chloro ethers (VI).



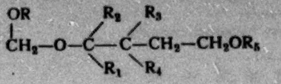
Organomagnesium compounds (II), prepared from γ-chloro ethers (I), react smoothly with aldehydes and ketones to yield magnesium chloroalkoxyalcoholates (III), which when treated with water yield 1,4-glycol monoethers (IV). However, in the experiments with acetophenone, together with compound (IV), a certain amount of methylphenylcarbinol and unsaturated ether is obtained, the formation of which can be explained on the basis on the basis of the free radical theory [2].

We synthesized the γ-chloro ethers (I) by the alkylation of α-chloro ethers with propylene and butylene [1]. As the carbonyl components we took acetaldehyde, benzaldehyde, acetone and acetophenone. In this manner we synthesized 17 new 1,4-glycol monoethers, the constants of which are given in Table 3.

By reacting various α-chloro ethers with magnesium chloroalkoxyalcoholates (III) by the method proposed by one of us [3], we synthesized 7 new δ-alkoxy derivatives of methylene glycol ether (ethers of δ-hydroxyacetals of formaldehyde) (see scheme), the constants of which are given in Table 1.

Reaction of the 1,4-diol monoethers (IV) with concentrated hydrochloric acid leads to replacement of the hydroxyl group on the tertiary carbon atom by chlorine with the formation of the corresponding δ-chloro ethers (VI). The reaction of replacing the hydroxyl by chlorine without the alkoxy group being attacked can to to completion only in the presence of a catalyst, a mixture of ammonium chloride and cuprous chloride. The constants of the obtained δ-chloro ethers are given in Table 2. An attempt to effect the reverse replacement of chlorine

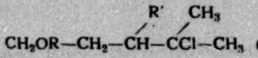
TABLE 1

δ-Alkoxy Derivatives of Methylene Glycol Ethers  (V)

$\overset{OR}{CH_2}-O-\underset{R_1}{\overset{R_2}{C}}-\underset{R_4}{\overset{R_3}{C}}-CH_2-CH_2OR_5$ (V)

Expt. nos.	R	R_1	R_2	R_3	R_4	R_5	Name of monoether
1	CH_3	CH_3	CH_3	H	CH_3	C_4H_9-n	Formaldehyde methyl (α,α-dimethyl-β-methyl-δ-butoxy) butyl acetal
2	C_5H_{11}-iso	CH_3	CH_3	H	CH_3	C_4H_9-n	Formaldehyde isoamyl (α,α-dimethyl-β-methyl-δ-butoxy) butyl acetal
3	CH_3	CH_3	CH_3	H	C_2H_5	CH_3	Formaldehyde methyl (α,α-dimethyl-β-ethyl-δ-methoxy) butyl acetal
4	C_2H_5	CH_3	CH_3	H	C_2H_5	C_2H_5	Formaldehyde ethyl (α,α-dimethyl-β-ethyl-δ-ethoxy) butyl acetal
5	C_4H_9-n	CH_3	CH_3	CH_3	CH_3	C_2H_5	Formaldehyde butyl (α,α-dimethyl-β,β-dimethyl-δ-ethoxy) butyl acetal
6	C_4H_9-n	CH_3	CH_3	CH_3	CH_3	C_4H_9-n	Formaldehyde butyl (α,α-dimethyl-β,β-dimethyl-δ-butoxy) butyl acetal
7	C_2H_5	C_6H_5	H	H	CH_3	C_4H_9-n	Formaldehyde ethyl (α-phenyl-β-methyl-δ-butoxy) butyl acetal

TABLE 2

δ-Chloro Ethers  (VI)

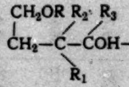
$CH_2OR-CH_2-\overset{R'}{CH}-\overset{CH_3}{CCl}-CH_3$ (VI)

Expt. nos.	Name of monoether	R	R′	Boiling point (pressure in mm)
1	1-Methoxy-4-methyl-3-ethyl-4-chloropentane	CH_3	C_2H_5	70—72° (11)
2	1-Ethoxy-4-methyl-3-ethyl-4-chloropentane	C_2H_3	C_2H_5	93—95 (10)
3	1-Butoxy-3,4-dimethyl-4-chloropentane	C_4H_9	CH_3	100—102 (6)
4	1-Isoamyloxy-3,4-dimethyl-4-chloropentane	C_5H_{11}	CH_3	102—103 (4)

Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		M		% C		% H		Yield (in %)
			found	calc.	found	calc.	found	calc.	found	calc.	
77.5—79° (10)	0.8984	1.4360	67.52	67.16	230.2	232	66.86	67.24	12.29	12.07	47.8
95—97 (9)	0.8453	1.4144	85.21	85.64	281.2	288	70.79	70.83	12.56	12.50	43.0
88—90 (24)	0.9236	1.4385	58.04	57.92	207.7	204	64.47	64.71	11.92	11.76	48.8
88—89 (15)	0.8670	1.4200	67.72	67.16	228.0	232	67.01	67.24	12.15	12.07	56.0
59—62 (4)	0.8475	1.4134	76.57	76.40	260.4	260	69.05	69.23	12.01	12.31	63.7
89—91 (3)	0.8550	1.4206	85.35	85.63	287.9	288	70.27	70.83	12.67	12.50	35.5
93—95 (36)	0.9916	1.4982	86.94	86.65	297.5	294	73.50	73.47	10.27	10.20	28.0

d_4^{20}	n_D^{20}	MR_D		M		Cl content (in %)		Yield (in %)
		found	calc.	found	calc.	found	calc.	
0.9435	1.4376	49.63	50.27	176.2	178.5	19.24	19.89	31.3
0.9214	1.4380	54.81	54.89	193.9	192.5	18.24	18.44	60.2
0.9120	1.4390	59.32	59.51	204.6	206.5	17.09	17.23	33.2
0.9047	1.4402	64.26	64.12	220.2	220.5	15.89	16.10	43.2

TABLE 3

1,4-Glycol Monoethers  (IV)

$$\mathrm{CH_2(CH_2OR)}-\mathrm{C}(R_1)(R_2)-\mathrm{COH}(R_3)-R_4$$

Expt. nos.	Name of monoether	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		M		% C		% H		% OH		Yield (in %)
					found	calc.	found	calc.	found	calc.	found	calc.	found	calc.	
1	1-Methoxy-3-methyl-4-pentanol	66—69° (4)	0.8917	1.4300	38.17	37.70	129.6	132	62.98	63.63	11.83	12.12	13.03	12.88	41.4
2	1-Ethoxy-3-methyl-4-pentanol	70—73 (3)	0.8947	1.4305	42.19	42.31	145.2	146	65.58	65.75	12.42	12.33	10.96	11.64	39.4
3	1-Butoxy-3-methyl-4-pentanol	90—91.5 (3)	0.8844	1.4330	51.00	51.55	174.2	174	68.72	68.96	12.63	12.65	10.23	9.77	33.5
4	1-Isoamyloxy-3-methyl-4-pentanol	87—89 (5)	0.8607	1.4210	55.39	56.10	186.4	188	70.04	70.21	12.80	12.76	9.50	9.04	31.6
5	1-Methoxy-3-ethyl-4-pentanol	76—78 (3)	0.9011	1.4310	41.94	42.31	144.2	146	65.70	65.75	12.36	12.33	12.10	11.64	44.67
6	1-Isoamyloxy-3-ethyl-4-pentanol	110—112 (5)	0.8592	1.4276	60.44	60.78	202.8	202	71.01	71.29	12.76	12.58	8.23	8.42	34.4
7	1-Methoxy-3,4-dimethyl-4-pentanol	66—67.5 (3)	0.9016	1.4360	42.34	42.31	147.9	146	65.79	65.75	12.06	12.33	11.90	11.64	36.06
8	1-Ethoxy-3,4-dimethyl-4-pentanol	76—78° (3)	0.8893	1.4436	47.75	46.93	163.3	160	67.27	67.50	12.46	12.50	10.47	10.62	34.3
9	1-Butoxy-3,4-dimethyl-4-pentanol	85—89 (3)	0.8897	1.4422	55.93	56.16	185.1	188	70.15	70.21	12.77	12.76	9.55	9.04	26.6
10	1-Isoamyloxy-3,4-dimethyl-4-pentanol	88—91 (3)	0.8730	1.4320	60.01	60.78	205.2	202	70.95	71.28	12.96	12.87	8.73	8.42	24.4
11	1-Butoxy-3-methyl-4-phenyl-4-butanol	83—85 (8)	0.9276	1.4748	71.60	71.74	235.2	236	76.14	76.27	10.14	10.17	7.42	7.20	57.5
12	1-Ethoxy-3-methyl-4-phenyl-4-pentanol	108—110 (18)	0.9643	1.4913	66.71	66.41	224.3	222	75.31	75.68	10.20	9.91	7.78	7.66	43.4
13	1-Butoxy-3,3-dimethyl-4-phenyl-4-pentanol	66—67 (3)	0.8890	1.4564	80.78	80.27	260.1	264	77.0	77.27	11.04	10.61	6.90	6.44	65.2
14	1-Methoxy-4-methyl-3-ethyl-4-pentanol	70—72 (3)	0.8999	1.4370	46.58	46.93	164.3	160	66.65	66.50	12.06	12.50	9.78	10.62	42.1
15	1-Butoxy-3,3,4-trimethyl-4-pentanol	102—103 (18)	0.8795	1.4392	60.43	60.78	198.4	202	71.21	71.29	12.36	12.87	9.15	8.42	32.6
16	1-Butoxy-3,3,4-trimethyl-4-pentanol	84—84.5 (2)	0.8702	1.4330	60.33	60.78	198.4	202	70.74	71.29	12.66	12.87	8.66	8.42	37.4
17	1-Isoamyloxy-4-methyl-3-ethyl-4-pentanol	80—83 (4)	0.8570	1.4300	65.11	65.40	213.0	216	72.11	72.22	12.92	12.96	7.50	7.87	30.7

by hydroxyl in the δ-chloro ethers proved unsuccessful. It was established that here even calcium carbonate cleaves HCl, leading to the formation of the unsaturated ether.

EXPERIMENTAL

Synthesis of 1-methoxy-3-methyl-4-pentanol (IV) (Table 1, compound 1). To the organomagnesium compound (II), prepared from 2.4 g of magnesium metal, 35 ml of ether and 13 g of methyl γ-chlorobutyl ether (I), was added 4.4 g of acetaldehyde with cooling. Then the stirring was continued for another 4 hrs at 40-45°. After standing for 8 hrs the complex was decomposed with slightly acid ice water. The reaction products were extracted from the lower layer with ether. The upper layer and the ether extract of the lower layer were combined, dried, the ether distilled off, and the residue vacuum-distilled twice.

Another 16 monoethers of type (IV) were synthesized in a similar manner (see Table 3).

Methyl (α,α,β-trimethyl-δ-butoxy)butyl ether of methylene glycol (V) (Table 1, compound 1) was obtained by reacting 8 g of methyl α-chloromethyl ether with the magnesium chloroalkoxyalcoholate (III) obtained from 16 g of butyl γ-chlorobutyl ether (I), 2.4 g of magnesium metal, 5.8 g of acetone and 40 ml of ether. The mixture was allowed to stand for 8 hrs, after which it was diluted with 50 ml of water. The upper layer was washed with 3% caustic solution, then with water, dried, and fractionally distilled in vacuo.

Six other new ethers of type (V) were synthesized in a similar manner (see Table 1).

δ-Chloro ethers (VI) were obtained in the following manner. To a mixture of 2.5 g of NH_4Cl, 1.25 g of Cu_2Cl_2 and 6 g of 1-methoxy-4-methyl-3-ethyl-4-pentanol (IV) was added 25 ml of concentrated hydrochloric acid (d 1.19) from a dropping funnel. After stirring for 2 hrs at room temperature the flask contents were diluted with an equal volume of water. The upper layer was washed with 3% caustic solution, then with water, and dried over Na_2SO_4. We isolated 2.4 g of 1-methoxy-4-methyl-3-ethyl-4-chloropentane (VI) (Table 2, compound 1).

Similar conditions were used to synthesize 3 other new δ-chloro ethers, the constants of which are given in Table 2.

SUMMARY

1. Seventeen new 1,4-diol monoethers of the aliphatic and aliphatic-aromatic series were synthesized and studied.

2. It was established that the organomagnesium method of synthesizing glycol ethers is suitable for the synthesis of the δ-alkoxy derivatives of methylene glycol ethers.

3. Seven new alkoxy derivatives of methylene glycol ethers were synthesized.

4. The hydroxyl group found at the tertiary carbon atom in 1,4-diol monoethers is easily replaced by chlorine when treated with concentrated hydrochloric acid in the presence of a catalyst (NH_4Cl + Cu_2Cl_2), leading to the formation of δ-chloro ethers.

5. Four new δ-chloro ethers were synthesized and studied.

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Received January 16, 1957

Azerbaidzhan State Pedagogical Institute

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* Original Russian pagination. See C. B. translation.

DIAMINES OF BENZIMIDAZOLE SERIES

I. SYNTHESIS AND PHYSICOCHEMICAL PROPERTIES OF DIAMINES

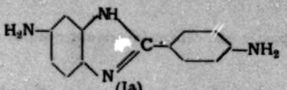
B. A. Porai-Koshits and Ch. Frankovskii

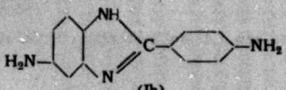
In this paper our purpose was to synthesize some diamines of the benzimidazole series and study their physicochemical properties.

The diamines of this series, as could be postulated on the basis of theoretical considerations and literature information, when diazotized and subjected to azo coupling, should give substantive dyes.

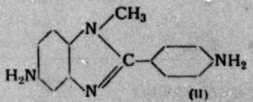
Little mention has been made in the literature relative to diamines of the benzimidazole series, and consequently it was necessary to develop a method for their preparation. It proved that the indicated diamines were easily synthesized by conventional methods (see experimental section).

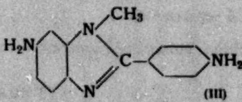
6(5)-Amino-2-p-aminophenylbenzimidazole (I), containing the imidazole ring, is a close analog of benzidine. Due to tautomerism, this diamine can have a second structure.


(Ia)


(Ib)

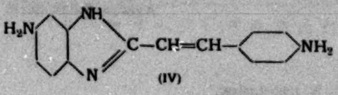
As can be seen from the formulas, the second tautomer fails to show conjugation between the amino groups. To determine which tautomer predominates in the usually obtained mixture, it was necessary to compare the properties of the latter with the properties of the two isomers (II) and (III) shown below.


(II)

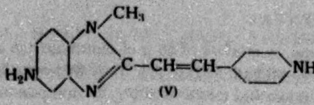

(III)

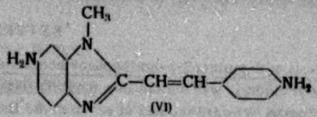
Judging by the similarity and difference in the properties, it becomes possible to arrive at a decision as to the structure of diamine (I).

Further, in order to follow the substantive properties shown by azo dyes derived from the diamines, it seemed of interest to lengthen the system of conjugated double and single bonds and to introduce the additional vinyl grouping between the terminal groups, i. e., the synthesis of diamine (IV) seemed in order.

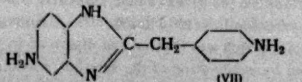

(IV)

In the same manner as before, this diamine should be compared with the analogous methylated diamines (V) and (VI), also differing from each other by the presence or absence of conjugation between the amino groups.


(V)


(VI)

In addition, it seemed of interest for the same reason to study the effect of introducing some other group, known to interrupt conjugation, in place of the vinyl grouping, for example, the methylene group (VII).


(VII)

Since most of the contemporary theories on substantivity associate this property with the presence of a conjugated system in dye molecules, and since, on the other hand, the reciprocal influence shown by amino groups in diamine molecules also depends on this conjugation, it was postulated that having studied the degree of conjugation found in diamine molecules, it then becomes possible to compare it with the magnitude of substantitivity shown by the azo dyes derived from the studied diamines. In our opinion, the degree of conjugation found in diamine molecules should be reflected on the values of their dissociation constants. For this reason we give the results of a physicochemical study of the above-mentioned diamines in this paper.

Basicity Constants of Synthesized Diamines

No. of diamine	$k_1 \cdot 10^9$	$k_2 \cdot 10^{11}$	$k_3 \cdot 10^{11}$
(I)	2.34	1.29	2.82
(II)	4.47	1.1	2.76
(III)	2.63	1.18	2.89
(IV)	1.99	1.63	3.52
(V)	3.99	1.91	3.99
(VI)	1.48	1.12	3.02
(VII)	1.82	6.03	6.31

Study of the principal properties of diamines of the benzimidazole series. The relationship between the reactivity of aromatic amines and their basicity constants in acylation and diazotization reactions, and in the formation of azomethines, diazo compounds and imidazole derivatives, was investigated earlier [1].

We decided to continue these studies in the direction of investigating the relationship that exists between the basicity constants of the diamines synthesized by us and their structure. The question as to the interrelationships existing between the basicity constants of the diamines (first and second), the degree of simultaneous diazotization shown by the two amino groups, etc. is an extremely complex one, and is of great theoretical and practical interest.

In the cases studied by us the relationship between the basicity constants and the structure is made even more complicated by the fact that the examined products have three basicity constants. Since for most of the studied diamines the first basicity constant is more or less constant, and at the same time is close to the value of the basicity constant of benzimidazole ($k \approx 1 \cdot 10^{-9}$), then obviously this constant should be regarded as belonging to the imidazole ring.

Consequently, the second and third constants should be regarded as belonging to the amino groups of the diamines studied by us. The potentiometric titration method was used to determine the basicity constants. The experimental results obtained by us are given in the table.

A comparison of the basicity constants of diamines (I) and(IV) with those of their alkyl derivatives could possibly give an answer to the question of the structure of diamines (I) and (IV). However, due to the greater basicity of the imidazole ring in comparison to the amino groups, it is the first to be involved in salt-formation. This salt-formation destroys the difference between the alkyl isomers, as a result of which the basicity constants of the amino groups in both the isomeric diamines and diamines (I) and (IV) are extremely close to each other.

Since these constants differ but slightly from the corresponding constants of diamine (VII), in which the presence of a methylene group is known to interrupt conjugation between the two amine groups, it must be assumed that salt-formation involving the imidazole ring leads in all cases to disruption of conjugation between the amino groups.

EXPERIMENTAL

Synthesis of 6-amino-2-p-aminophenylbenzimidazole. A mixture of 45 g of dinitroaniline and 45 g of p-nitrobenzoyl chloride was melted in a reaction flask in an oil bath at 180° [2]. Here hydrogen chloride was evolved copiously. Toward the end of reaction the temperature was raised to 200°; the temperature of the mass was held here for 15 min. On conclusion of reaction the obtained product was washed with acetone to remove starting substances and tarry products. Recrystallization from pyridine gave pale yellow needles of 2,4-dinitro-1-p-nitrobenzoylaniline with m. p. 195°. The yield was 70 g (81.4%).

2,4-Dinitro-1-p-nitrobenzoylaniline (43 g) was added gradually (reaction is vigorous) to a boiling solution of stannous chloride in 250 ml of hydrochloric acid (d 1.19). The reaction mass on cooling deposited the complex of the diamine with stannous chloride, which was filtered and dissolved in water. The tin was precipitated electrolytically. The precipitate, obtained by evaporation of the solution, was dissolved in a small amount of water and precipitated with ammonia. Recrystallization from water gave 6-amino-2-p-aminophenylbenzimidazole. M. p. 235-236° [2]. Yield of product 20.5 g (74%). The molecular weight of the 5(6)-amino-2-p-aminophenylbenzimidazole was determined by potentiometric titration and proved to be 223.1 (calculated 224).

Synthesis of 5-amino-1-methyl-2-p-aminophenylbenzimidazole. We synthesized 2,4-dinitrodimethylaniline by the Schuster method [3]. To oxidize this product to 2,4-dinitromethylaniline we used the Romburgh method [4], which consisted in treating the compound with chromic anhydride in acetic acid at the boil (for 1 part of 2,4-dinitrodimethylaniline we took 4 parts of glacial acetic acid and 1 part of chromic anhydride; reaction time 30-40 min, and yield 57.2%).

The obtained product was partially reduced to 4-nitro-2-aminomethylaniline by analogy with the reduction of 2,4-dinitroaniline, according to [5], i. e., by reduction with hydrogen sulfide in alcoholic ammonia medium. The yield of product was 64.8%. M. p. 177° (from alcohol). The obtained 2-amino-4-nitromethylaniline was converted to the imidazole derivative by condensation with p-nitrobenzoyl chloride in the following manner. A previously blended mixture of 15 g of 4-nitro-2-aminomethylaniline and 15 g of p-nitrobenzoyl chloride was placed in a porcelain beaker. The reaction mass was gradually heated in an oil bath to 170-180°. At 90° the mixture changed from a red to a yellow color, which apparently could be due to progress of acylation. Water began to be evolved at 160°, which indicates closure of the ring. The yield of 5-nitro-1-methyl-2-p-nitrophenylimidazole was 25.5 g (96%). It was obtained as yellow needles after recrystallization from pyridine. M. p. 272-273°.

Found %: N 18.99, 19.05. $C_{14}H_{10}O_4N_4$. Calculated %: N 18.79.

The obtained product was reduced in the same manner as in the previous case. To synthesize 5-amino-1-methyl-2-p-aminophenylbenzimidazole we took 10 g of 5-nitro-1-methyl-2-p-nitrophenylbenzimidazole, 140 g of stannous chloride and 100 ml of concentrated hydrochloric acid. The yield of 5-amino-1-methyl-2-p-aminophenylbenzimidazole was 7.1 g (88.5%). The product was purified by precipitation from hydrochloric acid with ammonia, followed by recrystallization from water. The product was obtained as brown needles. M. p. 203-204°.

Found %: N 23.62, 23.56. M (potentiometric) 233. $C_{14}H_{14}N_4$. Calculated %: N 23.53. M 238.

Synthesis of 6-amino-1-methyl-2-p-aminophenylbenzimidazole. The nitration was run by the Fitch method [6], and the oxidation by the Romburgh method, the latter in the same manner as had been described for the oxidation of 2,4-dinitrodimethylaniline. A mixture of 13 g of 2,5-dinitromethylaniline and 13 g of p-nitrobenzoyl chloride was blended by grinding in a mortar. The obtained mixture was fused in a porcelain beaker at 140°. On conclusion of reaction the yellow powder was isolated, and recrystallized from alcohol. Yield 25.5 g (81%). 2,5-Dinitro-1-methyl-1-p-nitrobenzoylaniline has m.p. 146°.

Found %: N 16.17, 16.25. $C_{14}H_{10}O_7N_4$. Calculated %: N 16.18.

The obtained product was reduced to 6-amino-1-methyl-2-p-aminophenylbenzimidazole by the above-described procedure. For the synthesis we took 18.9 g of 2,5-dinitro-1-methyl-1-p-nitrobenzoylaniline, 232 g of stannous chloride and 150 ml of hydrochloric acid (d 1.18). The yield of 6-amino-1-methyl-2-p-aminophenylbenzimidazole as the free base was 9.1 g (66.5%). The product was purified by recrystallization from water. M. p. 231°.

Found %: N 23.70, 23.72. $C_{14}H_{14}N_4$. Calculated %: N 23.53.

Synthesis of 5-amino-1-methyl-2-p-aminostyrylbenzimidazole. A mixture of 18 g of 5-nitro-1,2-dimethylbenzimidazole and 18 g of p-nitrobenzaldehyde, previously blended in a mortar, was placed in a porcelain beaker. The reaction mixture was heated in an oil bath to 180°. Water soon began to be evolved, which indicated the start of condensation. The liquid melt became solid toward the end of reaction. To complete the reaction the temperature was raised to 200°. The obtained hard melt was then ground to a powder. Yield of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole 31 g (83.4%). M. p. 262°. After recrystallization from pyridine, m. p. 278°.

Found %: N 17.03, 17.29. $C_{16}H_{12}O_4N_4$. Calculated %: N 17.26.

Into a liter flask, fitted with stirrer and condenser, was charged 300 ml of alcohol, 300 ml of hydrochloric acid (d 1.19), 225 g of stannous chloride and 28.5 g of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. The solution was heated to the boil and heated under reflux for 3 hrs. The precipitate gradually disappeared. At the end of reaction the solution was cooled, and the deposited complex salt of diamine with stannous chloride was filtered and then dissolved in water. The tin was precipitated electrolytically. The solution was evaporated to dryness. The residue was then dissolved in a small volume of water and precipitated with ammonia. The yield of 5-amino-1-methyl-2-p-aminostyrylbenzimidazole was 14.3 g (61.9%). After repeated precipitation of the diamine hydrochloride with ammonia the melting point of the free base rose to 218-219°.

Found %: N 21.06, 21.01. M (potentiometric) 272. $C_{16}H_{16}N_4$. Calculated %: N 21.20. M 264.

Synthesis of 1,2-dimethyl-6-nitrobenzimidazole.* 1,2-Dimethyl-6-nitrobenzimidazole was synthesized by the Phillips scheme [7], which we had studied in detail. 2-Methyl-5(6)-nitrobenzimidazole (190 g) was heated in methyl alcohol, containing hydrogen chloride in an amount equal to 75% of the benzimidazole. The reaction was run for 4 hrs at 160°. At the end of reaction the mass was treated with ammonia to separate from quaternary derivative, and then with alkali to remove starting product. We obtained 35 g of crude product. Recrystallization from alcohol raised the melting point to 195-210°, and then recrystallization from nitrobenzene raised it to 220-225°. The product was recrystallized 4 times. We obtained 7.5 g of 1,2-dimethyl-6-nitrobenzimidazole with m. p. 252-252.5° [7]. A mixture of this compound with the other pure isomer (5-nitro-1,2-dimethylbenzimidazole), having m. p. 225-226° (literature gives 226°), melted at 195-222°.

Found %: N 21.93, 22.13. $C_9H_9O_2N_3$. Calculated %: N 21.99.

Synthesis of 6-amino-1-methyl-2-p-aminostyrylbenzimidazole. For this synthesis we used the method described by A. E. Porai-Koshits [8] and O. Kym [2] for the synthesis of similar compounds. A mixture of 7 g of 1,2-dimethyl-6-nitrobenzimidazole and 7 g of p-nitrobenzaldehyde was placed in a reaction test tube and heated in an oil bath to 180°. Complete melting of the mass occurred at this temperature. The condensation reaction began at the same time, the start of which could be judged by the droplets of water collecting on the walls of the test tube. After holding at this temperature for 30 min the temperature was gradually raised (in 30 min) to 210°. As soon as the liquid melt turned solid, further heating could be stopped. Then the cooled dark-brown melt was ground to a powder and boiled with alcohol to remove unreacted starting substances. Yield of crude product 11.1 g (93.5%). M. p. 280-281°. The synthesized dinitro derivative is a bright yellow, finely crystalline compound that is insoluble in ether, alcohol, acetone and nitrobenzene. Recrystallization from hot pyridine gave 10.45 g of 6-nitro-1-methyl-2-p-nitrostytylbenzimidazole, m. p. 282.5-283.5°.

Found %: N 17.32, 17.45. $C_{16}H_{12}O_4N_4$. Calculated %: N 17.26.

The obtained dinitro derivative was then reduced with stannous chloride in a mixture of alcohol and hydrochloric acid by the method described above for the reduction of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. For the reduction we took 6 g of 6-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. The reduction solution on cooling and long standing deposited the complex salt of the diamine with tin (1st portion). Evaporation of the filtrate gave some more of the tin complex (2nd portion). Both portions of complex salt (each separately) were then dissolved in water, and the tin was precipitated electrolytically at a copper electrode (carbon anode). The solution, containing the diamine hydrochloride, was evaporated to dryness. Evaporation of the 1st portion yielded 5.6 g of the salt, while the 2nd portion yielded 3.4 g. Evidently the hydrochloride contains water of crystallization. Recrystallization from water, using bone charcoal for decolorization, gave 2.2 g of bright orange salt. The filtrates were collected, evaporated to dryness, and the residue was recrystallized from concentrated hydrochloric acid; another 3.8 g of salt was isolated here. The obtained salt does not melt even when heated to 340°, but only darkens. To obtain the free base a solution of the salt was treated with ammonia. Due to the fact that the diamine is easily oxidized, the solution of the salt was treated with hydrogen sulfide prior to precipitation with ammonia. To effect complete decomposition of the salt the solution was boiled with excess ammonia; 6-amino-1-methyl-2-p-aminostyrylbenzimidazole was obtained as a bright yellow product with m. p. 212-214°.

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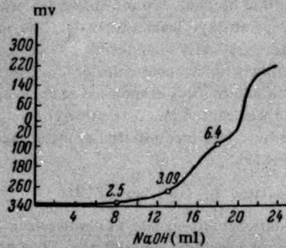
* The compound was synthesized by graduate student E. Zonis.

Found %: N 21.48, 21.13. M (potentiometric titration) 265. $C_{16}H_{16}N_4$. Calculated %: N 21.2. M 264.



Synthesis of 5(6)-amino-2-p-aminobenzylbenzimidazole. A mixture of 13 g of 2,4-dinitroaniline and 15 g of p-nitrophenylacetyl chloride was blended thoroughly and then melted in a reaction beaker at 120-140°. The reaction was run for about an hour. The resulting dark melt was then ground in a mortar. The yield of 2,4-dinitro-1-p-nitrophenylacetylaniline was 24.2 g (97.6%). Recrystallization from pyridine gave yellow crystals. M. p. 175°.

Found %: N 16.22, 16.19. $C_{14}H_{10}O_7N_4$. Calculated %: N 16.18.

The above-described procedure was used to reduce the obtained product to 6-amino-2-p-aminobenzylbenzimidazole. For the reduction we took 20 g of 2,4-dinitro-1-p-nitrophenylacetylaniline. The yield of free base was 8.7 g (48.7%). 6-Amino-2-p-aminobenzylbenzimidazole was reprecipitated several times from hydrochloric acid with ammonia, followed by recrystallization from water. The pure product has m. p. 223°.

Found %: N 23.40, 23.30. M (potentiometric) 246. $C_{14}H_{14}N_4$. Calculated %: N 23.5. M 238.

Potentiometric titration of the diamines—benzimidazole derivatives. A solution of 0.1 g of diamine in a mixture of 37.5 ml of ethyl alcohol and 37.5 ml of water was treated with 10-15 ml of 1 N hydrochloric acid. The solution prepared in this manner was titrated with 0.0952 N sodium hydroxide solution using an LP-4 potentiometer with glass electrode. In all cases the titration curve had two inflection points; one corresponded to titration of the excess hydrochloric acid, and the other corresponded to titration of the benzimidazole itself.

Calculation of the basicity constants, given in the table, was made from the semiequivalent points. As an example we have shown the potentiometric titration curve of 6-amino-2-p-aminophenylbenzimidazole (see figure).

SUMMARY

Diamines of the benzimidazole series, containing two amino groups in different benzene rings, have close basicity constants, independent of whether the amino groups are or are not found in conjugation. The reason for this phenomenon must be sought in the greater basicity of the imidazole ring when compared to the amino groups, as a result of which it is the first to be involved in salt-formation, and its transformation here into the onium ion leads to rupture of the conjugation between the amino groups.

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Received March 20, 1957

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DIAMINES OF BENZIMIDAZOLE SERIES

II. SUBSTANTIVE PROPERTIES OF THE AZO DYES DERIVED FROM THE DIAMINES

B. A. Porai-Koshits and Ch. Frankovskii

The affinity of dyes for fibers (substantivity) is quite a complex phenomenon, depending on many factors: the chemical structure of the dye and its physical properties, the nature of the fiber, the dyeing conditions, etc. According to a number of authors [1-4], one of the most important substantivity factors is the chemical structure of the dye, in particular, the length of the chain of conjugated bonds and the coplanarity of the molecule.

In studying the problem of the relationship between substantivity and coplanarity it has been impossible to determine by physical measurements whether coplanarity is present or absent; here the investigators have limited themselves only to theories, analogies, etc. Up to now it has not been conclusively shown that an angle exists between the two phenyl groups in benzidine. For substituted benzidines, a priori, it has been assumed without experimental proof that bulky substituents, introduced in the 2,2'-positions, take the benzene rings out of one plane [4]; the electronic effect of these substituents was not taken into consideration here, which in itself, independent of whether the molecule has a planar or a nonplanar structure, can shorten the chain length of the conjugated bonds to varying degree.

The present paper is a continuation of the investigations made by A. E. Porai-Koshits in the domain of substantive benzimidazole dyestuffs. In the opinion of A. E. Porai-Koshits, the benzimidazole ring is a strong chromophore, enhancing the substantive properties of a dye molecule. Consequently, it could be expected that benzimidazole dyestuffs will show quite high substantivity. In the previous communication [5] we described seven diamines of this series, defined their structure, and determined their basicity constants.

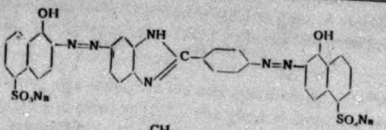
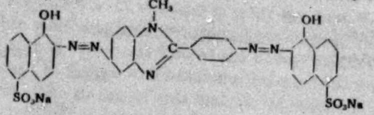
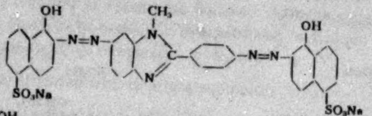
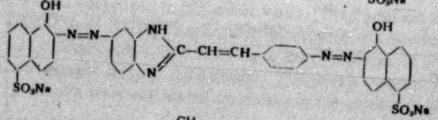
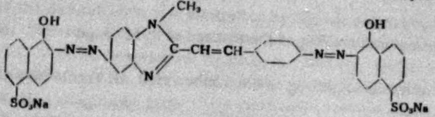
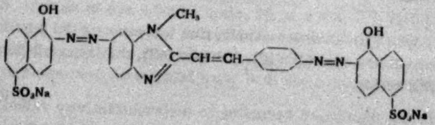
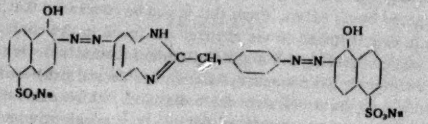
The direct purpose of the present study was to synthesize the azo dyes derived from the investigated diamines and study their substantivity properties. We took 1,5-naphthosulfonic acid as the azo component, and for some of the dyes we took naphthnoic,H-,J-,and Chicago-SS acids. Based on these examples, we followed the effect of diamine structure on the substantive properties of the dyes, and also the effect of the azo component on them.

The results of our experiments are summarized in Tables 1 and 2.

As we had already mentioned in the previous communication [5], the principal difference between the synthesized diamines of the benzimidazole series consists in the fact that some of them have conjugated chains of double and single bonds, and some do not have them. Thus, 6-amino-1-methyl-2-p-aminophenylbenzimidazole and 6-amino-1-methyl-2-p-aminostyrylbenzimidazole show an uninterrupted chain of double and single bonds between the amino groups, while in the diamines 5-amino-1-methyl-2-p-aminophenylbenzimidazole and 5-amino-1-methyl-2-p-aminostyrylbenzimidazole this chain is absent; finally, the diamines 5(6)-amino-2-p-aminophenylbenzimidazole and 5(6)-amino-2-p-aminostyrylbenzimidazole, because of possible isomerization, may or may not contain conjugated chains. Actually, the presence or absence of conjugation in the azo dyes synthesized by us from all of the above-enumerated diamines exerts a sharp influence on their substantivity values; thus, dye (III) proved to be more substantive than dye (II), and very close to dye (I) in its affinity value (see Table 1). The same also holds for the styryl derivative of benzimidazole; dyes (IV) and (VI) (see Table 1) proved to be more substantive than dye (V); here it should be mentioned that the substantivity of the styryl derivatives is greater than that of the phenyl derivatives of benzimidazole, since they possess a longer conjugation chain (compare dyes (IV) and (I), (V) and (II), and (VI) and (III); Table 1).

TABLE 1

Substantivity Values of Synthesized Dyes

Nos. of dyes	Dye	Substantivity (in %)
(I)		38
(II)		18
(III)		30
(IV)		40.8
(V)		24
(VI)		48
(VII)		10.3

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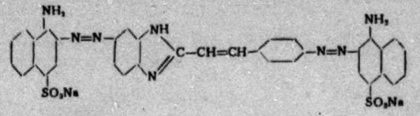
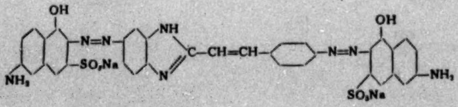
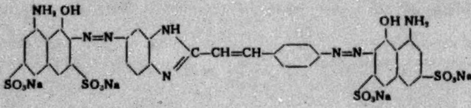
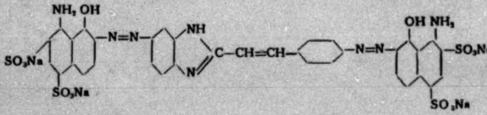
* The dyeings were made according to the method of D. G. Pereiaslova (in the presence of soda and salt).

TABLE 2

Substantivity Values of Synthesized Dyes

Nos. of dyes	Dye	Substantivity (in %)	
		A*	A**
(I)		9	53
(II)		27	—
(III)		9	66
(VI)		6.5	40

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* The dyeings were made according to the method of B. M. Bogoslovskii (in the absence of salt).

** The dyeings were made according to the method of D. G. Pereiaslova (in the presence of soda and salt).

As was to be expected, dye (VII), in which conjugation is broken by the introduction of a methylene group, proved to be much less substantive than dyes (I), (III), (IV) and (VI), the latter all possessing an uninterrupted chain of conjugated single and double bonds.

As regards dyes (I) and (IV), then based according to their substantivity values, they closely resemble dyes in which a long system of conjugated bonds exists. From this it can be concluded that in the indicated dyes the hydrogen atom of the benzimidazole ring is linked to the nitrogen not found in the conjugation chain. Apparently, a similar conclusion should be made regarding the original diamines themselves. We shall mention that a study of the basicity constants of 5(6)-amino-2-p-aminophenylbenzimidazole and 5(6)-amino-2-p-aminostyrylbenzimidazole failed to give us an answer to the structure of these diamines, which can vary because of tautomerism [5]. Consequently, determining the substantive properties of the azo dyes apparently proved to be a more precise study method, since it also permitted arriving at a conclusion as to the structure of the original diamines.

The above-enumerated facts indicate that a rule, similar to that observed for dyes of the benzidine series, also holds in the series of benzimidazole dyes. The character of the influence exerted by different azo-components on the substantivity value of a dye is also retained in going from the benzidine to the benzimidazole series. The dyes derived from J-acid are more substantive than the dyes derived from H-acid, while the dyes derived from H-acid are more substantive than the dyes derived from Chicago-SS acid (see Table 2). The question of the influence exerted by the sulfo group on substantivity must be considered unsolved.

EXPERIMENTAL

The dyes were synthesized in conventional manner. The obtained amines were diazotized with sodium nitrite solution in hydrochloric acid medium. For example, for a typical reaction we took 2.5 g of 6-amino-2-p-aminostyrylbenzimidazole, 30 ml of water, 4 ml of hydrochloric acid, and 1.4 g of sodium nitrite in 4 ml of water. The azo coupling was run in alkaline medium, as described below.

A mixture of 5 g of azurinic acid and 6.75 g of soda was dissolved in 50 ml of water; the obtained solution was cooled to 0°. The above-obtained diazo solution was added to this solution with constant stirring, keeping the temperature at 0-5°. The reaction course was controlled by means of either excess diazo-component or azo-component. To complete azo-coupling the reaction mass was stirred for 3 hrs. At reaction end all of the dyestuff was found as sodium salt in the precipitate. The filtrate had a slight yellow-green color, and further salting out failed to yield any more dyestuff.

The purity of the obtained dye was controlled chromatographically. The presence of any other dyes could not be shown. The dye was filtered and dried at 105°. The yield of technical product was 8.7 g. The benzidine method, first proposed by B. M. Bogoslovskii [4], was used to purify the dyestuff. The dyestuff was dissolved in water, heated to the boil, and then a hot solution of benzidine hydrochloride was added. This gave the salt of the dyestuff with benzidine as a precipitate, which was filtered and washed with cold water until the test for chloride ion was negative. After this the salt of the dye with benzidine was dried and weighed. The obtained salt was heated in soda solution for 20 min. The amount of soda used was calculated in advance; it was not more than 80% of the amount theoretically required to decompose the salt. Here the benzidine and traces of the benzidine salt of the dye deposited in the precipitate, while the dye remained in solution as the sodium salt. The solution was filtered through a fluted filter and then evaporated to dryness.

The dyes were analyzed by titration with titanium trichloride.

A 0.1 g sample of the dye was dissolved in 250 ml of water. Then a 50 ml aliquot of the solution was removed with a pipette, the aliquot treated with 25 ml of a 20% Rochelle salt solution, and the whole heated to the boil. The boiling solution was titrated with 0.0282 N $TiCl_3$ to the appearance of a yellow color (or decolorization), with constant passage of carbon dioxide through the solution. The excess titanium chloride was back-titrated with methylene blue solution. The results were calculated according to the procedure given in [7].

The purity of some of the dyestuffs was also controlled by the use of benzidine hydrochloride and by microanalysis for elemental sulfur. The substantivity was determined as the difference between the starting and final dye bath. We used the method of B. M. Bogoslovskii to make the dyeings: weight of cloth sample 1 g, concentration of sodium chloride solution 5 g/liter, amount of dye 4% on weight of cloth, bath ratio 1 : 40, time of dyeing 1 hr. Since some of the dyes coagulated under these conditions, we also used the dyeing method of D. G. Pereiaslova [6]: 1 g of cloth, amount of dye 0.00002 mole, 2% soda and 20% sodium chloride on weight of cloth, bath ratio 1 : 30, time of dyeing 1 hr, temperature 80°. Parallel experiments with blank baths containing only the dye solutions were run at the same time. The substantivity was expressed in percent of dyestuff absorbed. The concentrations of the dye baths were determined using both the colorimetric method and the method of titration with titanium trichloride.

SUMMARY

The dyes, formed from bis-diazotized diamines of the benzimidazole series and 1,5-naphtholsulfonic acid, show different substantivity depending on whether the azo groups are or are not in mutual conjugation. Based on the substantivity values of the obtained azo dyes it becomes possible to judge whether conjugation is present or absent between the amino groups of the original diamines taken for synthesis of the indicated dyes. The character of the influence exerted by other azo-components (for example, J-, H- or Chicago-SS acid) on the substantivity of the azo dyes discussed here is similar to that exerted in the benzidine dye series.

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Received March 20, 1957

Lensovet Technological Institute, Leningrad

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* In Russian.

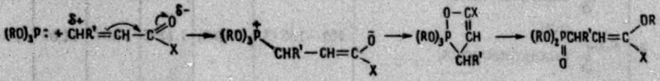
** Original Russian pagination. See C. B. translation.

ADDITION OF NEUTRAL ESTERS OF PHOSPHOROUS AND PHOSPHONOUS ACIDS TO CONJUGATED SYSTEMS

IV. ADDITION OF ESTERS OF PHENYLPHOSPHONOUS ACID TO α,β-UNSATURATED ALDEHYDES AND ACIDS

Gil'm Kamai and V. A. Kukhtin

In earlier communications [1] we described the reaction between trialkyl phosphites and compounds showing C=C−C=O conjugation.

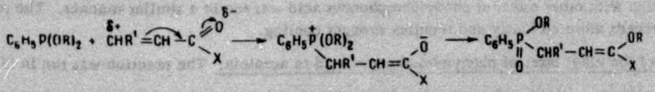


This reaction in its mechanism is similar to the reaction of alkyl halides with trialkyl phosphites, and can be regarded as one of the forms of the Arbuzov rearrangement.

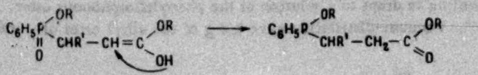
It could be expected that the esters of phenylphosphonous acid, reacting with alkyl halides and being more active than the trialkyl phosphites, would easily react with conjugated systems.

As our experiments revealed, the esters of phenylphosphonous acid actually do react very vigorously with α,β-unsaturated aldehydes and acids. Reaction here is much more vigorous than in the case of the trialkyl phosphites. Thus, for example, the esters of phenylphosphonous acid react with methacrylic acid with the evolution of heat, in which connection the temperature rises to 125-130° when the reactants are poured together slowly. The reaction with acrylic acid and with acrolein is even more vigorous. The addition products of phenylphosphonous esters to acrolein lend themselves with great difficulty to distillation even in a high vacuum; in this connection we were able to isolate only the addition product of the ethyl ester of phenylphosphonous acid to acrolein in the pure state. Since the reaction of α,β-unsaturated aldehydes and acids with phenylphosphonous esters proceeds more violently than in the case of the trialkyl phosphites, and is accompanied by a much greater evolution of heat, we were unable to confirm, even indirectly, the presence of an intermediate product in the Arbuzov rearrangement.

It is possible to depict the reactions studied by us by Scheme (A), and in the case of acids, where hydrogen migration occurs, by Scheme (B).



(A)

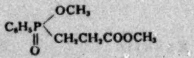
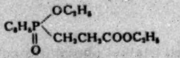
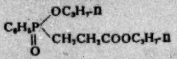
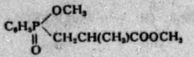
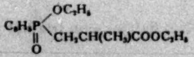
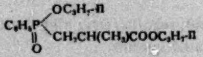
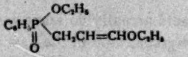


(B)

The constants of the ethyl ester of β-phenylphosphonoisobutyric acid obtained by us lie close to those described earlier by A. N. Pudovik [2].

The results obtained by us indicate that the conclusions of A. E. Arbuzov [3] relative to the reactivity of different esters of trivalent phosphorus with alkyl halides are also valid for other cases of the Arbuzov rearrangement, in particular, also for the case where systems with $C=C-C=O$ conjugation are involved.

The constants of the compounds synthesized by us are given in the table.

Expt. nos.	Formula	Boiling point (pressure in mm)	n^{20}_D	d^{20}_0	%P		Yield (in %)
					calc.	found	
1	 $C_6H_5P(=O)(OCH_3)CH_2CH_2COOCH_3$	159—160° (5)	1.5062	1.1591	12.81	12.63	40.4
2	 $C_6H_5P(=O)(OC_2H_5)CH_2CH_2COOC_2H_5$	178—179 (3)	1.5040	1.1532	11.48	11.42	51.5
3	 $C_6H_5P(=O)(OC_3H_7\text{-n})CH_2CH_2COOC_3H_7\text{-n}$	183—184 (5)	1.4995	1.0691	10.32	10.01	50.3
4	 $C_6H_5P(=O)(OCH_3)CH_2CH(CH_3)COOCH_3$	163—165 (5)	1.5046	1.1297	12.07	11.83	38.0
5	 $C_6H_5P(=O)(OC_2H_5)CH_2CH(CH_3)COOC_2H_5$	185—186 (8)	1.5000	1.1210	10.91	10.65	40.2
6	 $C_6H_5P(=O)(OC_3H_7\text{-n})CH_2CH(CH_3)COOC_3H_7\text{-n}$	188—190 (9)	1.5019	1.1261	9.93	9.68	32.5
7	 $C_6H_5P(=O)(OC_2H_5)CH_2CH=CHOC_2H_5$	150—152 (0.5)	1.5136	1.0389	12.18	11.88	11.2

EXPERIMENTAL

Addition of ethyl ester of phenylphosphonous acid to methacrylic acid. 10 g of ethyl phenylphosphonite was treated with 4.4 g of methacrylic acid. The temperature of the mixture quickly rose to 130°; to prevent further temperature rise the reaction flask was cooled with ice water. The reaction mass was cooled to room temperature and then heated for 1 hr at 130-134°. Vacuum-distillation gave 6.2 g (40.2%) of the ethyl ester of β-phenylphosphonoisobutyric acid.

B. p. 185-186° (8 mm); $n^{20}D$ 1.5000, d^{20}_0 1.1210, MR_D 74.50; calculated 74.12. Found %: P 10.65. $C_{14}H_{21}O_4P$. Calculated %: P 10.21.

The reaction with other esters of phenylphosphonous acid was run in a similar manner. The reaction with acrylic acid proceeds more violently and requires stronger cooling.

Addition of the ethyl ester of phenylphosphonous acid to acrolein. The reaction was run in dioxane.

3 g of acrolein was added with cooling in drops to a solution of the phenylphosphonous ester. The temperature during reaction was kept at 80-100°. Vacuum-distillation gave 1.4 g of the ethyl ester of γ-ethoxyallylphenylphosphonous acid.

B. p. 150-152° (0.5 mm); $n^{20}D$ 1.5136, d^{20}_0 1.0389. Calculated %: P 12.18. $C_{13}H_{19}O_3P$. Found %: P 11.88.

SUMMARY

The reaction between the esters of phenylphosphonous acid and α,β-unsaturated aldehydes and acids was studied. It was established that the esters of phenylphosphonous acid add to α,β-unsaturated aldehydes and acids in the same manner as the trialkyl phosphites.

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Received March 18, 1957

Kazan Institute of Chemical Technology

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* Original Russian pagination. See C. B. translation.

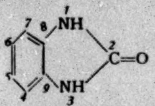
** In Russian.

IMIDAZOLE DERIVATIVES

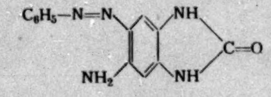
XX. SOME AMINO DERIVATIVES OF BENZIMIDAZOLONE

L. S. Efros and A. V. El'tsov

In studying the chemical properties of amino derivatives of benzimidazolone (I) we established [1] that the azo coupling of 5-aminobenzimidazolone with diazotized aniline takes place at carbon 6 of (II); 5-amino-1,3-dimethylbenzimidazolone behaves in exactly the same manner.



(I)



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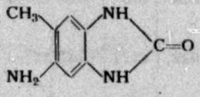


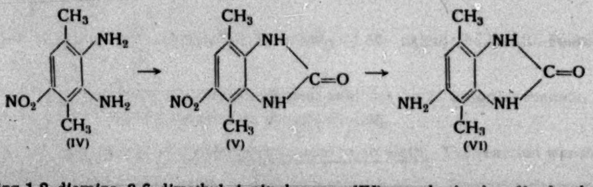
(III)

On the basis of this we postulated that under the influence of the imidazolone ring the electron cloud of the benzene ring in benzimidazolone is deformed in such manner that the double-bond character between carbon atoms 5 and 6 is greatly increased.

In order to determine the degree of this deformation we decided to synthesize two aminobenzimidazolones, one of which had the 6 position, and the other the 4 position, blocked by a methyl group, and to determine how these compounds would react with diazonium salts.

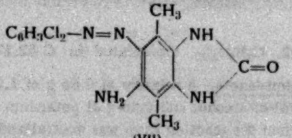
Starting with the earlier described [2] 6-methyl-5-nitrobenzimidazolone we synthesized 5-amino-6-methylbenzimidazolone (III), which failed to enter into azo coupling with all of diazo compounds tested by us, clear up to p-nitrophenyldiazonium chloride, and the solitary reaction product always proved to be the diazoamino compound.

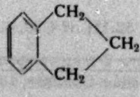
As the amine in which the carbon atom in position 4 was blocked we used 5-amino-4,7-dimethylbenzimidazolone (VI), synthesized by the scheme



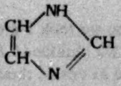
The starting 1,2-diamino-3,6-dimethyl-4-nitrobenzene (IV) was obtained earlier by the reduction of 2,4-dinitro-3,6-dimethylbenzazide [3]. The cited authors state that the same diamine can also be obtained by the partial reduction of 2,4-dinitro-3,6-dimethylaniline [4]. We employed the last method, running the reduction with sodium sulfide in alcohol medium. Treatment of diamine (IV) with carbon bisulfide in alkaline alcoholic medium gave us 4,7-dimethyl-5-nitro-2-mercaptobenzimidazole. The fusion of diamine (IV) with urea proceeds very smoothly and if (IV) is sufficiently pure the obtained nitro compound can be reduced without purification by recrystallization.

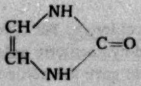
As we had anticipated, 5-amino-4,7-dimethylbenzimidazolone (VI) readily entered into azo coupling with diazotized aniline and 2,5-dichloroaniline; the last azo dye was purified and analyzed (VII). These facts serve as convincing evidence that in the benzene ring of benzimidazolone the double-bond linkage of positions 5-6 is substantially increased, while that of positions 4-5 and 6-7 is correspondingly decreased. Such a disruption of bond equality was postulated earlier only for the case of hydrindene (VIII) [5]; however, it was shown in later papers that this postulation is incorrect [6]. For this reason the observations presented by us here deserve special attention, while the conclusions derived from them deserve further experimental verification by both chemical and physical methods.

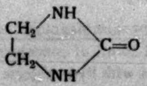

(VII)


(VIII)

To explain the imidazolone ring exerting such an influence on the benzene ring condensed with it, it is expedient to compare the chemical properties of imidazole (IX) and imidazolone (X) [7]. The first compound is characterized by having a clearly defined aromatic nature, whereas the second compound tends to migrate into derivatives of imidazolone (XI), adding hydrogen, halogens, etc.


(IX)


(X)


(XI)

The presence of a system of 6 π-electrons in imidazole (IX) and the absence of the same in imidazolone (X) leads to the situation that these heterocycles exert different influence on the benzene rings condensed with them. Imidazolone, striving to assume the more stable structure of imidazolidone (XI), in the benzo derivatives "forces out" the π-electrons of bonds 8-9 into the benzene ring (I), which leads to the manifested disruption of the equality of the bonds in the benzene ring of benzimidazolone. Imidazole strives to retain its aromatic structure, which is reflected in a "naphthalene-like" deformation of the electron cloud of the benzene ring in benzimidazole [8].

EXPERIMENTAL

2,4-Dinitro-3,6-dimethylaniline. A mixture of 70 g of trinitro-p-xylene and 1600 ml of alcohol was charged into a flask, fitted with reflux condenser and a tube for bubbling in gas, descending to the bottom of the flask. A fast stream of ammonia was passed through the solution for 3 hrs with simultaneous heating on the water bath. Then the mixture was heated for another hour at the boil, and then cooled. The obtained crystalline precipitate was filtered, washed on the filter with a small amount of alcohol, and dried. The crude product melts at 201° and can be used for subsequent work without further purification. Yield 65-70%. After one recrystallization from acetic acid the coarse yellow needles of 2,4-dinitro-3,6-dimethylaniline melted at 203°.

1,2-Diamino-3,6-dimethyl-4-nitrobenzene. A mixture of 12.3 g of finely divided 2,4-dinitro-3,6-dimethylaniline and 100 ml of alcohol was placed in a flask, fitted with stirrer, reflux condenser, thermometer and dropping funnel, and to this mixture at 55° and with vigorous stirring was added in drops a warm solution of 22 g of crystalline sodium sulfide in 20 ml of water at such a rate that the temperature did not exceed 65°. The addition of the sodium sulfide solution was accompanied by a rise in temperature; however, in some cases additional heating was required to initiate reaction. After all of the reducing agent had been added,the mixture was stirred vigorously at 65-70° for 15 min, and here the 2,4-dinitro-3,6-dimethylaniline went into solution. Then the dark-red solution was poured into a porcelain dish, acidified with hydrochloric acid until acid to Congo, and then evaporated on the water bath to dryness. The dry residue was treated twice with 100-ml portions of boiling dilute hydrochloric acid, the precipitate was filtered, and the mother liquors were neutralized with ammonia. The obtained precipitate of diamine was filtered, for purification was reprecipitated twice from dilute hydrochloric acid with ammonia, and then dried. Yield 4-6.3 g. The product melts at 166° and can be used without further purification. One recrystallization from alcohol gave the diamine with m. p. 169°, which agrees with the literature [3].

4,7-Dimethyl-5-nitrobenzimidazolone. A mixture of 5.8 g of 1,2-diamino-3,6-dimethyl-4-nitrobenzene and 11.5 g of urea was ground in a mortar, after which the mixture was heated in a porcelain crucible in an oil bath at 200-205° for 1 hr. Here the liquid melt solidified with the evolution of ammonia. Then the crucible was cooled and the contents dissolved in 200 ml of dilute caustic solution, the solution boiled with carbon, the carbon removed by filtration, and the dark-red filtrate neutralized with acid. The obtained precipitate was filtered and then recrystallized from glacial acetic acid. We obtained 4.8 g of compound. Fine yellow-green needles, not melting at 325°.

Found %: C 52.48, 52.11; H 4.89, 4.82. $C_9H_9O_3N_3$. Calculated %: C 52.17; H 4.38.

4,7-Dimethyl-5-nitro-2-mercaptobenzimidazole. A mixture of 0.65 g of 1,2-diamino-3,6-dimethyl-4-nitrobenzene, 0.5 ml of carbon bisulfide, 10 ml of alcohol and 0.46 g of potassium hydroxide was heated in a flask fitted with reflux condenser for 3 hrs. Then the reaction mass was neutralized with acetic acid and evaporated in vacuo to dryness. The residue was reprecipitated from dilute alkali with acid, and then recrystallized from a large volume of alcohol. We obtained 0.3 g of substance as a dirty-yellow amorphous powder, not melting at 325°.

Found %: S 14.36, 14.50. $C_9H_9O_2N_3S$. Calculated %: S 14.36.

The amino derivatives were obtained by reducing the nitro products, as had already been described in a previous communication [1].

5-Amino-6-methylbenzimidazolone hydrochloride. For reaction we took 1 g of 5-methyl-6-nitrobenzimidazolone, 1.5 g of tin and 10 ml of concentrated hydrochloric acid. We obtained 0.8 g of the amine hydrochloride. Reprecipitation from water with hydrochloric acid gave the compound as coarse rhombic crystals, containing a molecule of water, and not having a sharp melting point.

Found %: C 44.21; H 5.72; N 19.44, 19.52. $C_8H_9ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 44.14; H 6.02; N 19.31.

The picrate also does not have a good melting point and decomposes completely at 260°.

4,7-Dimethyl-5-aminobenzimidazolone hydrochloride. For reaction we took 2.8 g of the nitro derivative, 40 ml of concentrated hydrochloric acid and 5 g of tin. The hydrochloride of the amine crystallized from water as fine colorless needles. After two recrystallizations we obtained 2 g of substance, containing a molecule of crystallization water.

Found %: N 18.14, 18.39; Cl 15.71, 15.70. M 235, 229. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: N 18.14; Cl 15.30. M 231.

5-Amino-4,7-dimethyl-6-(2,5-dichlorophenylazo)benzimidazolone. A solution of 0.25 g of 4,7-dimethyl-5-aminobenzimidazolone hydrochloride in 20 ml of water was treated with a solution of 0.4 g of the double salt of the diazo compound from 2,5-dichloroaniline with zinc chloride in 10 ml of water. After 15 min the precipitate was filtered, recrystallized from aqueous pyridine, then treated with boiling 4% acetic acid, and finally washed with water. Red powder, melting at 315°.

Found %: N 20.16, 20.04. $C_{15}H_{13}ON_5Cl_2$. Calculated %: N 20.00.

SUMMARY

5-Amino-6-methylbenzimidazolone is incapable of azo coupling, whereas 5-amino-4,7-dimethylbenzimidazolone reacts with diazo compounds to yield azo dyes. These observations support the validity of the earlier made conclusion that in the benzimidazolone molecule, under the influence of the nonaromatic imidazolone ring, the dual bonding of positions 5-6 is enhanced and the dual bonding of positions 4-5 and 6-7 is weakened.

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Received March 11, 1957

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* Original Russian pagination. See C. B. translation.

ORGANOMAGNESIUM SYNTHESIS AND PROPERTIES OF 1,1,1-TRIPHENYLALKYLMETHANES, 1,5-DIPHENYL-3-BENZYLPENTANE, AND 1-PHENYL-3-(2-PHENYLETHYL)TRIDECANE. II

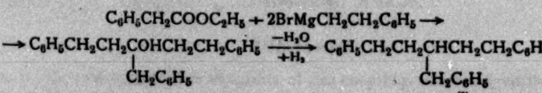
M. A. Chel'tsova, A. D. Petrov, and Iu. P. Egorov

Earlier [1] we had described the synthesis of a number of triphenylalkylmethanes, obtained by the scheme: $(C_6H_5)_3CCl + RMgX \rightarrow (C_6H_5)_3CR$ and it showed that the melting (freezing) points decrease with increase in the length of the radical R, both for solid hydrocarbons of the triphenylalkylmethane series and for their liquid perhydrides, the tricyclohexylalkylmethanes. In the present investigation we continued the synthesis of these series of hydrocarbons up to $R=C_{10}H_{21}$, and it was found that in the triphenylalkylmethane series the minimum freezing point occurs at $R=C_7H_{15}$ (Table 3). With further increase in the chain length the melting (freezing) points of the hydrocarbons in this series begin to rise again. At the same time, in the $(C_6H_{11})_3CR$ series they continue to fall at both $R=C_9H_{19}$ and $R=C_{10}H_{21}$ (to be sure, these last two hydrocarbons congeal to a glass).

The UV-absorption spectra, obtained for both the normal triphenylalkylmethanes and the branched triphenylalkylmethanes with a methylene group located in either the β- or γ-position to the central carbon atom, proved to be similar. One of these spectra is shown in Fig. 1,b. When compared with the spectrum of triphenylmethane (Fig. 1, c) it becomes possible to discern their similarity, not only in the location of the band and its shape, but also in the close intensity. From these data it follows that the triphenylmethane group is a quite stable chromophore, and is not materially affected by the length and degree of branching of the hydrocarbon chain. This conclusion could have been expected, since a similar phenomenon also exists for other aromatic alkyl derivatives, for example, the alkylbenzenes and alkylnaphthalenes.

In contrast to the β- and γ-methyl derivatives and the triphenyl-n-alkylmethanes, the α-methyl derivative $(C_6H_5)_3C-\underset{\overset{|}{C}}{C}(C)_6$ possesses a UV-spectrum that differs in both the shape and intensity of the band (Fig. 1,a). It is possible to assume that this difference is due to steric factors, as a result of which the CH_3 group disturbs the usual reaction of the aromatic rings through the C atom, i. e., it leads to some change in the electron levels of the system.

A second problem of our investigation was to study the effect of spreading the phenyl rings, i. e., of casting them from one carbon atom (which is the case, for example, with the 1,1,1-triphenylalkanes) to the terminal carbon atoms of the triphenylalkane chains (structures that are characterized by having the lowest freezing points), on the freezing points of triphenyl- and diphenylalkanes. For this we synthesized hydrocarbon (I) with composition $C_{24}H_{26}$, namely



$$C_6H_5CH_2COOC_2H_5 + 2BrMgCH_2CH_2C_6H_5 \rightarrow$$
$$\rightarrow C_6H_5CH_2CH_2\underset{\underset{CH_2C_6H_5}{|}}{C}OHCH_2CH_2C_6H_5 \xrightarrow[+H_2]{-H_2O} C_6H_5CH_2CH_2\underset{\underset{CH_2C_6H_5}{|}}{C}HCH_2CH_2C_6H_5$$

(I)

1,5-diphenyl-3-benzylpentane, which had the quite high m. p. of +55°, but which obviously was still approximately 50° lower than the m. p. of the isomeric hydrocarbon 1,1,1-triphenylhexane (the melting point of $C_{23}H_{24}$ is 153°, and that of $C_{25}H_{28}$ is +76°).

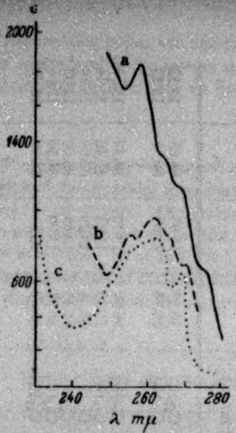


Fig. 1. UV-spectra of triphenylalkylmethanes in 2,2,4-trimethylpentane solution.

a – $(C_6H_5)_3$ C–C–C, b – $(C_6H_5)_3CC_6H_{19}$, c – $(C_6H_5)_3CH$.

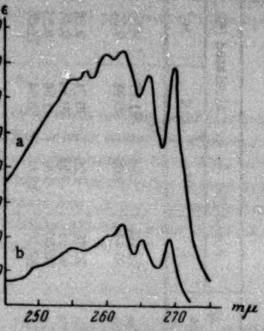


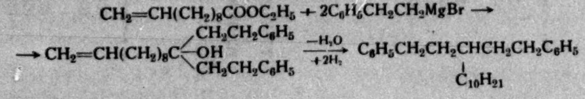
Fig. 2. UV-Spectrum of 1,5-diphenyl-3-benzylpentane. a) In 2,2,4-trimethylpentane solution, b) ethylbenzene.

The high freezing point of the indicated hydrocarbon, whereas its closest homolog (differing only by a CH_2 group) 1,5-diphenyl-3-(2-phenylethyl) pentane f. p. −32° [2], caused us at first to consider the possible cyclization of the olefin to the hydrindan derivative when it was hydrogenated under pressure. However, as the spectral study discussed below revealed, this derivative is absent.

Even in isooctane solution in the UV-spectra of the triphenylmethane compounds have a very diffuse character. The absorption bands almost do not have a fine structure. In this respect they differ from the monosubstituted aromatic compounds, in which this structure is well defined. The spectrum obtained for (I) shows a distinct fine structure, and in its shape and position of maxima the absorption band corresponds to that of a monosubstituted aromatic ring (Fig. 2).

Two UV-absorption curves are shown in Fig. 2: (a) is that of the investigated compound, and (b) is of ethylbenzene. In (a) we observe an approximately 3-fold increase in band intensity and the retention, as had already been indicated above, of a fine structure. This indicates that here we are dealing with three widely separated aromatic rings, in accordance with the postulated structure. The possible formation of an indan structure is indicated in the literature [3]; however, if we refer to the UV-spectrum of such a compound, it becomes possible to establish that the first maximum of its band is located at 273 mμ with an intensity of 1800 units. In our spectrum this portion shows an intensity of only 200 units, and any indication of an absorption band is completely lacking. Consequently, the formation of such a compound in noticeable amount must be rejected.

After all three rings had been hydrogenated, the resulting 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane had f. p. −20°. Tricyclohexylbutylmethane has f. p. +50° (crystals). Evidently, here also a spreading of the cyclohexyl rings made it possible to lower the freezing point by 50°. The effect of spreading the rings proved to be even more pronounced in the case of diphenylalkanes. Using the scheme given below, we synthesized hydrocarbon (II), 1-phenyl-3-(2-phenylethyl) tridecane ($C_{27}H_{40}$), which proved to have a freezing point of −60°. From the literature [4] it is known that 1,1-diphenyltetradecane ($C_{26}H_{38}$) has melting point +17.9°.



$$CH_2{=}CH(CH_2)_8COOC_2H_5 + 2C_6H_5CH_2CH_2MgBr \longrightarrow$$

$$\longrightarrow CH_2{=}CH(CH_2)_8C(OH)(CH_2CH_2C_6H_5)_2 \xrightarrow[+2H_2]{-H_2O} C_6H_5CH_2CH_2\underset{\displaystyle C_{10}H_{21}}{\underset{|}{C}H}CH_2CH_2C_6H_5$$

(II)

TABLE 1

Physicochemical Properties of Triphenyl- and Diphenylalkanes

Formula	Boiling point (pressure in mm)	d_4^{40}	n_D^{40}	MR_D		Empirical formula	Found (%)		Calculated (%)	
				found	calc.		C	H	C	H
$(C_6H_5)_3CC_7H_{15}$	220° (4)	1.0036	1.5730	112.3	111.5	$C_{26}H_{30}$	91.10	8.85	91.17	8.83
$(C_6H_5)_3C\underset{\displaystyle CH_3}{\underset{\vert}{C}}HC_6H_{13}$	207—208 (3)	0.9960	1.5662	117.3	116.1	$C_{27}H_{32}$	90.44	9.00	90.94	9.01
$(C_6H_5)_3CC_9H_{19}$	189—190 (2)	0.9842	1.5620	121.75	120.76	$C_{28}H_{34}$	90.78	9.20	90.74	9.26
$(C_6H_5)_3CC_{10}H_{21}$	248—249 (3)	—	—	—	—	$C_{29}H_{36}$	90.35	9.55	90.56	9.45
$(C_6H_5CH_2CH_2)_2CHCH_2C_6H_5$	171—172 (1)	—	—	—	—	$C_{24}H_{26}$	90.60	9.62	91.66	8.34
$(C_6H_5CH_2CH_2)_2CHC_{10}H_{21}$	176—177 (1)	0.9154 (20°)	1.5169 (20°)	120.3	119.7	$C_{27}H_{40}$	89.36	10.66	88.94	11.06

TABLE 2

Physicochemical Properties of Tricyclohexyl- and Dicyclohexylalkanes

Formula	Boiling point (pressure in mm)	d_4^{40}	n_D^{40}	MR_D		Empirical formula	Found (%)		Calculated (%)	
				found	calc.		C	H	C	H
$(C_6H_{11})_3CC_4H_9$	168—169 (0.5)	—	—	—	—	$C_{23}H_{42}$	86.97	12.95	86.68	13.32
$(C_6H_{11})_3C\underset{\displaystyle CH_3}{\underset{\vert}{C}}HC_6H_{13}$	166—167 (0.5)	0.9269	1.5035	119.65	120.21	$C_{27}H_{50}$	86.74	13.07	86.51	13.49
$(C_6H_{11})_3CC_9H_{19}$	200—201 (3)	0.9167	1.4980	124.5	124.90	$C_{28}H_{52}$	86.65	13.40	86.49	13.51
$(C_6H_{11})_3CC_{10}H_{21}$	175—176 (1)	0.9119	1.4980	129.4	129.5	$C_{29}H_{54}$	86.35	13.24	86.46	13.54
$(C_6H_{11}CH_2CH_2)_2CHCH_2C_6H_{11}$	194—195 (1)	0.9035*	1.4920*	106.65	106.46	$C_{24}H_{44}$	86.62	13.29	86.66	13.34
$(C_6H_{11}CH_2CH_2)_2CHC_{10}H_{21}$	216—217 (1)	0.8995*	1.4800*	122.98	122.49	$C_{27}H_{52}$	86.45	13.65	86.08	13.92
$(C_6H_{11})_2CHC_9H_{19}$	146—147 (3)	0.8879*	1.4820*	99.57	99.40	$C_{22}H_{42}$	86.34	13.70	86.16	13.84
$(C_6H_{11})_2CH\underset{\displaystyle CH_3}{\underset{\vert}{C}}HC_6H_{13}$	156—157 (4)	0.9090*	1.4960*	93.82	94.78	$C_{21}H_{40}$	86.40	13.57	86.08	13.92

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* At 20°.

The melting points and viscosities of the triphenyl-, diphenyl-, tricyclohexyl- and dicyclohexylalkanes that we synthesized in the present study are given in Table 3. Other physical properties of these hydrocarbons and their elemental analysis data are given in Tables 1 and 2.

EXPERIMENTAL*

The triphenylchloromethane taken for reaction was purified to constant melting point by repeated recrystallization, and the bromides were purified by 2-3 distillations through a column having an efficiency of 20 theoretical plates at 20-40 mm. The yields of the hydrocarbons ranged from approximately 20 to 30%. About 100-150 g of each hydrocarbon was prepared. To effect complete hydrogenation the triphenylalkanes were hydrogenated under pressure over Raney-Ni at 150-170°. 1,1-Dicyclohexyl-2-methyloctane and 1,1-dicyclohexyldecane were isolated in the hydrogenation of 1,1,1-triphenyl-2-methyloctane and 1,1,1-triphenyldecane, being obtained as the result of one ring cleaving from the starting hydrocarbons during hydrogenation.

TABLE 3

Melting Points and Viscosities of Triphenyl-, Diphenyl-, Tricyclohexyl- and Dicyclohexylalkanes

Formula	Melting (freezing) point	Viscosity (in centistokes)				
		0°	20°	50°	100°	150°
$(C_6H_5)_3CC_7H_{15}$	+15 gl.	—	—	572.0	15.0	3.7
$(C_6H_5)_3C\underset{\underset{CH_3}{\mid}}{CH}C_6H_{13}$	+15 gl.	—	—	422.0	15.8	4.9
$(C_6H_5)_3CC_9H_{19}$	30 cryst.	—	—	91.0	8.2	2.9
$(C_6H_5)_3CC_{10}H_{21}$	42 cryst.	—	—	92.0	10.6	3.3
$(C_6H_5CH_2CH_2)_2CHCH_2C_6H_5$	55 cryst.	—	—	—	—	—
$(C_6H_5CH_2CH_2)_2CHC_{10}H_{21}$	—60 gl.	—	12.1	4.4	—	—
$(C_6H_{11})_3CC_4H_9$	50 cryst.	—	—	—	—	—
$(C_6H_{11})_3CC_4H_9$-iso	47 cryst.	—	—	—	—	—
$(C_6H_{11})_3CC_7H_{15}$	+10 gl.	—	—	635.0	19.4	3.2
$(C_6H_{11})_3C\underset{\underset{CH_3}{\mid}}{CH}C_6H_{13}$	+ 2 gl.	—	—	431.0	16.5	4.0
$(C_6H_{11})_2C_9H_{19}$	+ 3 gl.	—	—	133.6	8.2	4.4
$(C_6H_{11})_2CC_{10}H_{21}$	— 5 gl.	—	—	130.0	12.1	3.4
$(C_6H_{11}CH_2CH_2)_2CHCH_2C_6H_{11}$	—20 gl.	—	501.5	48.4	7.0	2.4
$(C_6H_{11}CH_2CH_2)_2CHC_{10}H_{21}$	—50 gl.	170.9	47.5	18.3	14.5	2.07
$(C_6H_{11})_2CHC_9H_{19}$	—10 gl.	169.3	44.9	10.8	2.6	1.4

1,5-Diphenyl-3-benzylpentane. Here 1-bromo-2-phenylethane, one of the starting products, was obtained by us in 90% yield using the method of [5], i. e., by the slow distillation of 2-phenylethanol with 48% HBr. B. p. 105° (18 mm), $n^{20}D$ 1.5570, d^{20}_4 1.3643. From [6], b. p. 99° (15 mm), $n^{20}D$ 1.5572 (yield 92%). We obtained 350 g of phenylacetic acid (m. p. 74-75°) from 750 g of benzyl chloride, from which we prepared 170 g of the ethyl ester with b. p. 188° (11 mm), $n^{20}D$ 1.5020, d^{20}_4 1.0314. From [7], b. p. 227.1° (760 mm), $n^{18.5}D$ 1.4992, d^{20}_4 1.0333. From 170 g of ethyl phenylacetate and $C_6H_5CH_2CH_2MgBr$ (from 430 g of $C_6H_5CH_2CH_2Br$) we obtained 88 g (30%) of 1,5-diphenyl-3-benzyl-3-pentanol.

B. p. 263° (5 mm), 225° (1 mm), $n^{20}D$ 1.5855, d^{20}_4 1.0658, MR_D 103.90; calculated 103.75. Found %: C 87.77; H 7.94; OH 5.4. $C_{24}H_{26}O$. Calculated %: C 87.22; H 7.94; OH 4.0.

We used the procedure of [8] to dehydrate 1,5-diphenyl-3-benzyl-3-pentanol. A mixture of 88 g of the carbinol, 140 g of glacial acetic acid and 1 ml of conc. H_2SO_4 was heated on the water bath for 30 min, after which the unsaturated hydrocarbon was isolated in conventional manner.

B. p. 206-207° (2 mm), d^{20}_4 1.0307, $n^{20}D$ 1.5890 (yield 53%), MR_D 102.93; calculated 101.76. Found %: C 92.18; H 7.87. $C_{24}H_{24}$. Calculated %: C 92.25; H 7.75.

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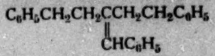
* V. P. Krukhtanova and I. N. Lifanova assisted in the experimental portion of this investigation.

An exaltation of 1.17 units makes it possible to assume that the hydrocarbon has the structure of (III).



$$C_6H_5CH_2CH_2\underset{\underset{CHC_6H_5}{\|}}{C}CH_2CH_2C_6H_5$$

(III)

The hydrocarbon (22 g) was first hydrogenated under pressure at 100-120° over Bag catalyst [9]. Here a product with m. p. 55° was obtained. To effect complete hydrogenation, 22 g of the unsaturated hydrocarbon was hydrogenated under pressure at 150-170° over Raney-Ni. The naphthenic hydrocarbon obtained here had f. p. −20°.

1-Phenyl-3-(2-phenylethyl) tridecane. 1-Phenyl-3-(2-phenylethyl)-12-tridecen-3-ol was obtained in 82% yield from $C_6H_5CH_2CH_2MgBr$ (from 215 g of $C_6H_5CH_2CH_2Br$) and 122 g of ethyl undecylenate.

B. p. 263° (4 mm), d^{20}_4 0.9585, $n^{20}D$ 1.5315, MR_D 122.2, calculated 122.8. Found %: C 86.33; H 10.19; OH 4.48. $C_{27}H_{36}O$. Calculated %: C 86.65; H 10.12; OH 4.49.

The compound was dehydrated in the same manner as indicated above for 1,5-diphenyl-3-benzyl-3-pentanol. We obtained 107 g (60%) of mixed dienic hydrocarbons from 178 g of the carbinol.

B. p. 195 (1 mm), d^{20}_4 0.9364, $n^{20}D$ 1.5307. MR_D 119.05; calculated 118.75. Found %: C 89.72; H 10.10. $C_{27}H_{36}$. Calculated %: C 89.92; H 10.08.

45 g of the dienic hydrocarbon mixture was hydrogenated under pressure at 100° over Bag catalyst. We obtained 36 g of hydrogenated product. The hydrocarbon had f. p. −60° (its structurally similar 1-phenyl-3-(2-phenylethyl) undecane freezes at −54° and has d^{20}_4 0.9215 and $n^{20}D$ 1.5192). 30 g of the mixed dienic hydrocarbons was hydrogenated under pressure at 150-170° over Raney-Ni. We obtained 24 g (91.7%) of 1-phenyl-3-(2-phenylethyl)-tridecane.

SUMMARY

1. Fourteen new hydrocarbons were synthesized [1,1,1-triphenyloctane, 1,1,1-triphenyl-2-methyloctane, 1,1,1-triphenyldecane, 1,1,1-triphenylundecane, 1,5-diphenyl-3-benzylpentane, 1-phenyl-3-(2-phenylethyl) tridecane, 1,1,1-tricyclohexylpentane, 1,1,1-tricyclohexyl-2-methyloctane, 1,1,1-tricyclohexyldecane, 1,1,1-tricyclohexylundecane, 1,1-dicyclohexyl-2-methyloctane, 1,1-dicyclohexyldecane, 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane and 1-cyclohexyl-3-(2-cyclohexylethyl) tridecane, and their melting (freezing) points and viscosities were determined.

2. It was shown that in the triphenylalkylmethane series both the viscosity and freezing point decrease with increase in the length of the alkyl chain up to C_7H_{15}, after which they begin to increase again. Apparently, a similar minimum also exists in the tricyclohexylalkylmethane series, but here it could not be fixed due to the fact that both the tricyclohexylnonyl- and -decylmethanes congeal to a glass.

3. It was found that transition from 1,1,1-tricyclohexylpentane to 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane and from 1,1-diphenyltetradecane to 1-phenyl-3-(2-phenylethyl) tridecane results in substantial decrease in the freezing points, being caused by a spreading of the cyclohexyl (phenyl) rings in the hydrocarbon molecules.

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Received March 18, 1957

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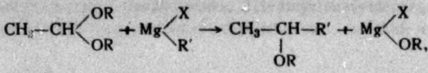
REACTION OF EXCHANGE OF HYDROXYL GROUPS FOR RADICALS OF ORGANOMAGNESIUM COMPOUNDS

II. REACTION OF GRIGNARD REAGENT WITH SYMMETRIC ACETALS

M. F. Shostakovskii and M. R. Kulibekov

In the previous paper [1] we studied the reactivity of mixed acetals when reacted with Grignard reagent and established that here it is the heavier hydroxy radical of the mixed acetal that exchanges for the radical of the organomagnesium compound. At the same time it was shown that the alkyl aryl acetals are highly reactive in this sense.

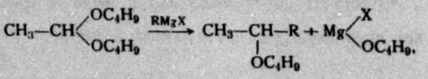
As a continuation of this study, we set out to investigate the reaction of Grignard reagent with symmetric acetals of the aliphatic, aliphatic-aromatic and aromatic series, and to develop methods for the synthesis of the corresponding ethers, some of them being difficultly accessible. In addition, it was of interest to study the specific influence exerted by different radicals in the Grignard reagent on the exchange reaction with symmetric acetals. As regards the reactivity of symmetric acetals, then on the basis of experimental data it is possible for us to state that in contrast to the mixed acetals they show a number of peculiarities, associated with the fact that both of the hydroxy radicals are the same. This creates a certain equilibrium in the molecule, which when disturbed results in exchange proceeding very smoothly by the scheme



$$CH_3-CH\begin{matrix}OR\\OR\end{matrix} + Mg\begin{matrix}X\\R'\end{matrix} \rightarrow CH_3-\underset{OR}{\underset{|}{CH}}-R' + Mg\begin{matrix}X\\OR\end{matrix},$$

where R = Alk, Ar or aralkyl radical.

Although a number of statements exist in the literature [2] on the exchange of alkoxyl groups by radicals of organomagnesium compounds, still they all fail to touch upon the problems associated with the course of the exchange reaction. For study we took three groups of symmetric acetals, namely the dialkyl, diaryl and sym. diaralkyl acetals. The dialkyl acetals taken for study were the dibutyl and diethyl acetals. When dibutyl acetal was reacted with butylmagnesium bromide, isoamylmagnesium bromide, benzylmagnesium chloride and phenylmagnesium bromide, in all cases one of the butoxy groups was replaced by the indicated radicals of the Grignard reagent to yield the corresponding ether



$$CH_3-CH\begin{matrix}OC_4H_9\\OC_4H_9\end{matrix} \xrightarrow{RMgX} CH_3-\underset{OC_4H_9}{\underset{|}{CH}}-R + Mg\begin{matrix}X\\OC_4H_9\end{matrix}.$$

where: R = n-C_4H_9, iso-C_5H_{11}, $CH_2C_6H_5$ or C_6H_5.

When dibenzyl acetal was reacted with isoamylmagnesium bromide, benzylmagnesium chloride and phenylmagnesium bromide, it was found that in contrast to the dialkyl acetals the exchange reaction proceeds with somewhat greater difficulty, i. e., drastic reaction conditions are required, which we were able to achieve by running the reaction without solvent at elevated temperature (110-120°). Under these conditions one of the benzyloxy groups is replaced by radicals of the Grignard reagent to yield the corresponding ethers. When diphenyl acetal is reacted with butylmagnesium bromide the exchange reaction proceeds with great vigor to yield the corresponding phenyl ether of 2-hexanol. For this reason the reaction was run under milder conditions than before, i. e., it was run by adding the diphenyl acetal to an ether solution of the organomagnesium compound. Based on the experimental data, we established that the ability of hydroxy radicals to exchange decreases in the order: $OC_6H_5 > OAlk > OCH_2C_6H_5$. Some of the constants of the ethers synthesized by us are given in the table.

EXPERIMENTAL

1. Reaction of dibutyl acetal with isoamylmagnesium bromide. 30 g of dibutyl acetal with b. p. 184.5° (747 mm), d^{20}_4 0.8257, $n^{20}D$ 1.4074, heated in a boiling water bath, was treated with an ether solution of isoamylmagnesium bromide, prepared from 8 g of magnesium and 50 g of isoamyl bromide. In order to raise the temperature of the reaction mixture the diethyl ether was distilled off as fast as it was added to the reaction flask. Heating was continued for about 2 hrs after all of the organomagnesium compound had been added. When all of the diethyl ether had been distilled off, the product developed intense self-heating (frothing) inside the reaction flask. The reaction product was decomposed with water, acidulated with acetic acid. If unreacted organomagnesium was absent, the decomposition with water went slowly with very little heat evolution. After decomposition, the oily product was separated from the water layer, washed with 10% HCl solution to hydrolyze any unreacted acetal, and then taken up in ether. The ether solution was washed with water, then with dilute soda solution, again with water, and finally it was dried over anhydrous sodium sulfate. The ether was distilled off on the water bath. The residue was distilled at atmospheric pressure; the following fractions were obtained at a pressure of 735 mm:

1st fraction, b. p. 74-158° (several drops); 2nd fraction, b. p. 159-175°, 1.5 g; 3rd fraction, b. p. 176-182°, 12 g; 4th fraction, b. p. 183-184°, 3 g.

The 4th fraction was unreacted acetal. The 3rd fraction was redistilled; here we obtained 10 g (50.8%) of the butyl ether of 2-methyl-5-hexanol, being a mobile, colorless, clear liquid with a fruity odor, insoluble in water, and readily soluble in organic solvents. Three other ethers were synthesized in a similar manner. The constants of all of the synthesized ethers are given in the table.

2. Reaction of diethyl acetal with phenylmagnesium bromide. Under the conditions of Expt. 1 we added the phenylmagnesium bromide, obtained from 3 g of magnesium and 19 g of bromobenzene, to 15 g of diethyl acetal. The reaction product was vacuum-distilled (12 mm). The following fractions were obtained: 1st fraction, b. p. 45-72°, 1.5 g; 2nd fraction, 73-82°, 9.5 g; residue 1.5 g.

Redistillation of the 2nd fraction from sodium gave 7 g (57.3%) of a liquid with b. p. 81-82° (13 mm), $n^{20}D$ 1.4905, d^{20}_{20} 0.9282. This product corresponds to the ethyl ether of 1-phenylethyl alcohol, which, according to the literature [1], has b. p. 185-187° and $d^{21.9}$ 0.931.

3. Reaction of dibenzyl acetal with isoamylmagnesium bromide. To the isoamylmagnesium bromide, obtained from 3 g of magnesium and 18 g of isoamyl bromide, heated after removal of the ether to 110°, was added 12 g of dibenzyl acetal. After mixing, the reactant mixture was heated for 1.5 hrs at 120°. The product was isolated in conventional manner and then vacuum-distilled. Redistillation from sodium metal gave 5 g (50%) of the benzyl ether of 2-methyl-5-hexanol. It was obtained as a colorless clear liquid with aromatic odor, insoluble in water, and readily soluble in organic solvents.

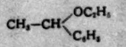
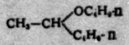
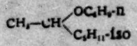
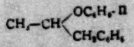
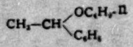
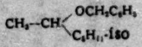
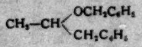
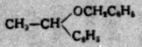
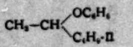
B. p. 129-131° (15 mm), $n^{20}D$ 1.4790, d^{20}_4 0.9001, MR_D 64.90; calculated 64.89. Found %: C 81.48, 81.30; H 10.61, 10.61. $C_{14}H_{22}O$. Calculated %: C 81.55; H 10.67.

The dibenzyl acetal for the given synthesis was obtained by us for the first time in good yield by heating butyl benzyl acetal in the presence of hydrochloric acid.

B. p. 184.5-185° (13 mm), $n^{20}D$ 1.5394, d^{20}_4 1.0500. MR_D 72.25; calculated 72.17. Found %: C 79.07, 78.89; H 7.51, 7.55. $C_{16}H_{18}O_2$. Calculated %: C 79.33; H 7.44.

Dibenzyl acetal is a colorless, clear, oily liquid with a slight odor. It is insoluble in water, and readily soluble in organic solvents. Two other ethers were synthesized by us under the above given conditions (see table).

4. Reaction of diphenyl acetal with butylmagnesium bromide. In constrast to the previous experiments this reaction was run in ether medium. To the butylmagnesium bromide, obtained from 3 g of magnesium and

Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Found (%)		Calc. (%)		Literature data
				found	calc.	C	H	C	H	
 $CH_3{-}CH\begin{smallmatrix}OC_2H_5\\C_6H_5\end{smallmatrix}$	81—82 (13)	1.4905	0.9282	—	—	— —	— —	—	—	B. p. 185—187°, $d^{21.0}$ 0.931 [1]
 $CH_3{-}CH\begin{smallmatrix}OC_4H_9\text{-n}\\C_4H_9\text{-n}\end{smallmatrix}$	169—171 (740)	1.4096	0.7883	50.06	50.02	76.73, 76.68	14.00, 14.08	76.94	13.92	
 $CH_3{-}CH\begin{smallmatrix}OC_4H_9\text{-n}\\C_5H_{11}\text{-iso}\end{smallmatrix}$	176—178 (735)	1.4133	0.7817	54.89	54.64	77.02, 76.81	13.95, 14.05	76.74	13.95	
 $CH_3{-}CH\begin{smallmatrix}OC_4H_9\text{-n}\\CH_2C_6H_5\end{smallmatrix}$	132—134 (20)	1.4897	0.9109	60.87	60.55	81.74, 81.64	10.20, 10.10	81.25	10.41	
 $CH_3{-}CH\begin{smallmatrix}OC_4H_9\text{-n}\\C_6H_5\end{smallmatrix}$	119—120 (14)	1.4840	0.9100	—	—	— —	— —	—	—	B. p. 220—225° (730), d_4^{20} 0.9063, n_D^{20} 1.4832 [3]
 $CH_3{-}CH\begin{smallmatrix}OCH_2C_6H_5\\C_5H_{11}\text{-iso}\end{smallmatrix}$	129—131 (15)	1.4790	0.9001	64.90	64.89	81.48, 81.30	10.61, 10.61	81.55	10.67	
 $CH_3{-}CH\begin{smallmatrix}OCH_2C_6H_5\\CH_2C_6H_5\end{smallmatrix}$	178—179 (14)	1.5430	1.0365	69.52	68.76	83.45, 83.66	7.73, 7.75	84.09	7.96	
 $CH_3{-}CH\begin{smallmatrix}OCH_2C_6H_5\\C_6H_5\end{smallmatrix}$	175—177 (20)	1.5552	1.0249	66.40	65.91	83.93, 83.77	7.59, 7.55	83.90	7.54	
 $CH_3{-}CH\begin{smallmatrix}OC_6H_5\\C_4H_9\text{-n}\end{smallmatrix}$	129—132 (29)	1.4964	0.9304	55.93	55.66	80.91, 80.28	9.76, 9.82	80.80	10.11	

17 g of butyl bromide, without distilling off the ether, was added 10 g of the acetal, and the whole heated on the water bath. Here the reaction mixture showed strong frothing and changed completely to a white solid mass. After decomposition, the product was isolated and vacuum-distilled (15 mm). The following fractionswere obtained: 1st fraction, b. p. 82-86°, 3 g; 2nd fraction, b. p. 87-116°, 2.5 g; 3rd fraction, 117-137°, 4.5 g.

The 1st and 2nd fractions reacted with sodium and had a phenolic odor. The 3rd fraction, reactiong weakly with sodium, was redistilled to give the phenyl ether of 2-hexanol. Clear colorless liquid with a slight odor. Insoluble in water, and readily soluble in organic solvents.

B. p. 129-132° (29 mm), $n^{20}D$ 1.4964, d^{20}_4 0.9304, MR_D 55.93; calculated 55.66. Found %: C 80.91, 80.28; H 9.76, 9.82. $C_{12}H_{18}O$. Calculated %: C 80.80; H 10.11.

SUMMARY

1. A study was made of the reaction for the exchange of the hydroxy radicals of symmetric acetals by radicals of the Grignard reagent.

2. The behavior of different hydroxy radicals in the exchange reaction was shown. It was found that the phenoxy group enters easiest into the exchange reaction, and that aralkoxy radicals exchange with the greatest difficulty. Alkoxy groups occupy a middle position.

3. Synthesized for the first time were the butyl ethers of 2-methyl-5-hexanol, 2-phenylpropyl alcohol and 1-phenylethyl alcohol, the benzyl ethers of 2-phenylpropyl alcohol and 1-phenylethyl alcohol, the phenyl ether of 2-hexanol, and dibenzyl acetal.

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Received March 21, 1957

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Institute

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* Original Russian pagination. See C. B. translation.

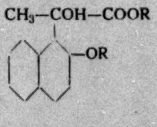
STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XVIII. SYNTHESIS OF ESTERS OF α-(β-ALKOXY-1-NAPHTHYL) LACTIC ACIDS

I. I. Lapkin and V. Ia. Vlasova

In studying the reactions of esters of α-keto acids with mixed organomagnesium compounds it was found by Grignard [1] that when the reactants are taken in equivalent proportions it is the more active keto group that reacts, and only when the Grignard reagent is taken in excess does the ester group react. Later studies added some modifications to this general rule. It was established by one of us [2] that esters of organic acids weaker than oxalic acid either do not react or react only slightly with arylmagnesium halides that contain alkyl radicals in the ortho-position. Later it was shown [3] that the ester group found in esters of α-keto acids, being acids weaker than oxalic acid, does not react with di-o-substituted arylmagnesium halides, and even with a large excess of the Grignard reagent only the keto group reacts, as a consequence of which the esters of tertiary α-hydroxy acids are the solitary reaction product. This method was used to synthesize such interesting and broadly important compounds as the esters of α-(β-alkoxy-1-naphthyl) lactic acids.

As is known, the naphthalene ring shows a number of properties that differentiate it from the benzene ring. Of these properties it is most important to mention the high reactivity shown by the carbon atom in the α-position. Together with this, the second ring in naphthalene is stereochemically almost equivalent to one ortho-substituent, attached to the benzene ring and creating steric hindrance. A system also stereochemically almost equivalent to a benzene ring with two ortho-substituents is obtained when an alkoxyl group is present in the β-position of the naphthalene ring. For this reason organomagnesium compounds, obtained from α-bromo-β-methoxy- and α-bromo-β-ethoxynaphthalene, react with the esters of pyruvic acid in exactly the same manner as the di-o-substituted arylmagnesium halides, i. e., with the formation of esters of α-(β-methoxy-1-naphthyl)- and α-(β-ethoxy-1-naphthyl) lactic acids of general formula (I).



(I)

The activity of the α-carbon atom in the naphthalene ring is reflected in a comparatively greater yield of reaction products. Our experimental results are given in the table.

EXPERIMENTAL

Reaction between the esters of pyruvic acid and the organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, was accomplished using the conventional conditions for Grignard reactions. Since the bromides proved to be comparatively insoluble in anhydrous ether we used a 50-50 volume mixture of toluene and ether, as the solvent. As had already been indicated, organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, are stereochemically similar to di-o-substituted arylmagnesium halides, for which reason the order of mixing the reactants is not important. In all of the experiments the starting compounds were taken in $^1/_8$ mole amounts. The time of heating the reaction mixture was 2 hrs. The Grignard complex was decomposed with 10% acetic acid. After solvent removal by distillation the product was purified by vacuum-distillation,

Reactants (1 : 1)	Formula of ester*	Yield (in %)	Boiling point (pressure in mm)	Melting point	Empirical formula	Content (in %)							
						C		H		OH		OR	
						found	calc.	found	calc.	found	calc.	found	calc.
2-Methoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(2-methoxy-1-naphthyl) lactate	35	182—184° (5)	110°	$C_{15}H_{16}O_4$	69.14	69.21	6.39	6.20	5.8	6.5	21.8	23.8
2-Methoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethyl α-(2-methoxy-1-naphthyl) lactate	58	186—188 (5)	107	$C_{16}H_{18}O_4$	69.99	70.05	6.72	6.61	5.5	6.2	—	—
2-Methoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(2-methoxy-1-naphthyl) lactate	63	200—202 (4)	61—62	$C_{18}H_{22}O_4$	71.25	71.50	7.16	7.32	5.3	5.6	—	—
2-Methoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(2-methoxy-1-naphthyl) lactate	57	201—203 (5)	66—67	$C_{18}H_{22}O_4$	71.63	71.50	7.24	7.32	5.2	5.6	—	—
2-Ethoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(2-ethoxy-1-naphthyl) lactate	32	208—210 (10)	131—132	$C_{16}H_{18}O_4$	69.78	70.05	6.48	6.61	6.0	6.2	—	—
2-Ethoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethoxy α-(2-ethoxy-1-naphthyl) lactate	50	203—205 (5)	90—91	$C_{17}H_{20}O_4$	70.53	70.81	6.90	6.99	5.1	5.9	27.6	31.2
2-Ethoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(2-ethoxy-1-naphthyl) lactate	61	207—209 (5)	33—34	$C_{19}H_{24}O_4$	72.26	72.12	7.56	7.65	5.0	5.4	—	—
2-Ethoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(2-ethoxy-1-naphthyl) lactate	55	199—201 (4)	61—62	$C_{19}H_{24}O_4$	71.91	72.12	7.71	7.65	5.3	5.4	—	—

followed by recrystallization from a mixture of petroleum ether and toluene (2:1). That reaction was normal was evidenced by the fact that all of the synthesized esters of α-(2-methoxy-1-naphthyl) lactic acid when saponified with 5% alcoholic KOH solution are converted to the same α-(2-methoxy-1-naphthyl) lactic acid. M. p. 155° (from aqueous alcohol). Not described in the literature.

Found %: C 68.09; H 5.52; OH 13.2; OCH_3 11.1. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73; OH 13.8; OCH_3 12.6.

Saponification of the esters of α-(2-ethoxy-1-naphthyl) lactic acid gave α-(2-ethoxy-1-naphthyl) lactic acid, which after recrystallization from aqueous alcohol had m. p. 184-185° (with decomp.). This acid is also new in the literature.

Found %: C 69.05; H 6.11; OH 12.0; OC_2H_5 15.9. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 13.1; OC_2H_5 17.3.

SUMMARY

It was established that the mixed organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, being stereochemically similar to di-o-substituted arylmagnesium halides, react in a similar manner with esters of pyruvic acid, i. e., only with the keto group, and not with the ester group, and it was also established that the formation of esters of α-(2-alkoxy-1-naphthyl) lactic acids is the final step in the indicated reaction.

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[1] V. Grignard, Compt. rend. 135, 627 (1902).

[2] I. I. Lapkin, J. Gen. Chem. 17, 1339 (1947).

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Received March 2, 1957

Perm State University

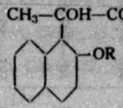
STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XIX. SYNTHESIS OF ESTERS OF α-(4-ALKOXY-1-NAPHTHYL) LACTIC ACID

I. I. Lapkin and O. M. Lapkina

In previous communications [1, 2] we had shown that when esters of α-keto acids, the latter being comparatively weak acids (in comparison to oxalic acid [3]), are reacted with di-ortho-substituted arylmagnesium halides, it is only the keto group that reacts; even with a large excess of the organomagnesium compound the ester group is not reactive here. It was also shown that the mixed organomagnesium compounds, obtained from α-bromo-β-alkoxynaphthalenes, stereochemically being compounds almost equivalent to di-ortho-substituted arylmagnesium halides, react only with the keto group. The organomagnesium compounds, obtained from 1-bromo-4-alkoxynaphthalenes, are stereochemically analogous to mono-ortho-substituted arylmagnesium halides, and for this reason behave in a similar manner [1] when reacted with esters of α-keto acids (pyruvic acid), i. e., they also react only with the more active keto group.

This circumstance can be utilized to conveniently synthesize the esters of α-(4-alkoxy-1-naphthyl) lactic acids of general formula (I). This is supported by the experimental results summarized in the table.



(I)

EXPERIMENTAL

The following conditions were used to react the esters of pyruvic acid with the mixed organomagnesium compounds, obtained from 1-bromo-4-alkoxynaphthalenes. To the activated magnesium, contained in a flask and covered with anhydrous ether, was added the bromide, dissolved in three volumes of ether. The bromide was taken in $^1/_7$ mole amount in all of the experiments. The pyruvic ester, dissolved in an equal volume of ether, was then slowly added to the prepared organomagnesium compound, and here a copious yellow precipitate usually formed in the flask. The mixture was heated for 2 hrs, and then decomposed in conventional manner with water and 10% acetic acid. The ether layer was separated from the aqueous layer, washed with water, then with 10% soda solution, and again with water until neutral. After removal of the solvent by distillation, the product was vacuum-distilled, purified to constant melting point by recrystallization from a mixture of toluene and petroleum ether, and analyzed.

All of the synthesized esters of α-(4-alkoxy-1-naphthyl) lactic acids were saponified with 5% alcoholic KOH solution. Saponification of the esters of α-(4-methoxy-1-naphthyl) lactic acid gave α-(4-methoxy-1-naphthyl) lactic acid. M. p. 130-132° (from toluene).

Found %: C 68.40; H 5.68; OH 13.6; OCH_3 10.8. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73; OH 13.8; OCH_3 12.6.

Recrystallization of the acid from either water or 30% alcohol gave the hydrate of this acid. M. p. 102-103°.

Reactants (1 : 1)	Formula of ester*	Yield (in %)	Boiling point (pressure in mm)	Melting point	Empirical formula	Content (%) C found	C calc.	H found	H calc.	OH found	OH calc.	OR found	OR calc.
4-Methoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(4-methoxy-1-naphthyl) lactate	38	187—189° (6)	117—118°	$C_{15}H_{16}O_4$	68.97	69.21	6.11	6.20	6.2	6.5	21.1	23.8
4-Methoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethyl α-(4-methoxy-1-naphthyl) lactate	60	191—193 (6)	75—76	$C_{16}H_{18}O_4$	69.83	70.05	6.60	6.61	5.6	6.2	—	—
4-Methoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(4-methoxy-1-naphthyl) lactate	56	212—214 (7)	72—73	$C_{18}H_{22}O_4$	71.21	71.60	7.31	7.32	5.2	5.6	—	—
4-Methoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Iosbutyl α-(4-methoxy-1-naphthyl) lactate	45	205—207 (6)	73—74	$C_{18}H_{22}O_4$	71.32	71.50	7.22	7.32	5.3	5.6	—	—
4-Ethoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(4-ethoxy-1-naphthyl) lactate	36	191—193 (6)	119—120	$C_{16}H_{18}O_4$	69.90	70.05	6.83	6.61	5.9	6.2	—	—
4-Ethoxy-1-naphthylmagnesium bromide + ethyl pyrivate	Ethyl α-(4-ethoxy-1-naphthyl) lactate	58	188—190 (4)	80—81	$C_{17}H_{20}O_4$	70.61	70.81	7.02	6.99	5.6	5.9	27.1	31.2
4-Ethoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(4-ethoxy-1-naphthyl) lactate	54	212—214 (6)	64—65	$C_{19}H_{24}O_4$	71.85	72.12	7.59	7.65	5.1	5.4	—	—
4-Ethoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(4-ethoxy-1-naphthyl) lactate	40	191—193 (3)	103—104	$C_{19}H_{24}O_4$	72.15	72.12	7.45	7.65	5.2	5.4	—	—

Found %: C 63.44; H 6.02. $C_{14}H_{14}O_4 \cdot H_2O$. Calculated %: C 63.63; H 6.11.

Saponification of the esters of α-(4-ethoxy-1-naphthyl) lactic acid gave α-(4-ethoxy-1-naphthyl) lactic acid. M. p. 168-170° (from toluene).

Found %: C 69.00; H 6.08; OH 11.8; OC_2H_5 15.3. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 13.1; OC_2H_5 17.3.

Recrystallization from either water or 30% alcohol gave the hydrate of this acid. M. p. 101-102°.

Found %: C 64.52; H 6.41. $C_{15}H_{16}O_4 \cdot H_2O$. Calculated %: C 64.73; H 6.52.

Both of the above acids are new in the literature.

The esters of pyruvic acid, used in the reactions, were obtained by heating pyruvic acid with an excess of the anhydrous alcohols, followed by the slow removal by distillation of the formed water and excess alcohol. Methyl pyruvate, b. p. 135-136°. Ethyl pyruvate, b. p. 54° (18 mm). Butyl pyruvate:*

B. p. 69° (12 mm), $d^{18.5}_4$ 0.9926, $n^{18.5}_D$ 1.4165, MR_D 36.49; calculated 36.19. Found %: C 58.13; H 8.30. $C_7H_{12}O_3$. Calculated %: C 58.31; H 8.39.

Isobutyl pyruvate:*

B. p. 67° (14 mm), $d^{18.5}_4$ 0.9873, $n^{18.5}_D$ 1.4131, MR_D 36.42; calculated 36.19. Found %: C 58.15; H 8.32. $C_7H_{12}O_3$. Calculated %: C 58.31; H 8.39.

SUMMARY

It was established that the method of preparing esters of α-aklyl- and aryllactic acids by reacting organomagnesium compounds with esters of pyruvic acid is entirely suitable for the synthesis of esters of α-(4-alkoxy-1-naphthyl) lactic acids.

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[1] I. I. Lapkin and A. I. Golovkova, J. Gen. Chem. 18, 485 (1948).

[2] I. I. Lapkin and V. Ia. Vlasova, J. Gen. Chem. 28, 955 (1958).**

[3] I. I. Lapkin, J. Gen. Chem. 17, 1339 (1947).

Received March 2, 1957

Perm State University

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* New compound.

** Original Russian pagination. See C. B. translation.

HETEROCYCLIC COMPOUNDS

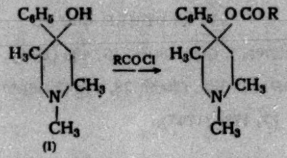
61. SYNTHETIC ANALGESIC SUBSTANCES

XXV. ESTERS OF 1,2,5-TRIMETHYL-4-PHENYL(ARYL)-4-PIPERIDOL

I. N. Nazarov,* N. S. Prostakov, and N. N. Mikheeva

In previous communications [1] we had described the synthesis of various esters of 1,2,5-trimethyl-4-phenyl-(aryl)-4-piperidols, and had shown that the character of the physiological action of these compounds depends to a large degree on the nature of the acyl radical. The esters of the aliphatic acids are usually analgesics, whereas the esters of the aromatic and aliphatic-aromatic acids prove to be local anesthetics.

To study the influence of the structure of esters of 1,2,5-trimethyl-4-phenyl-4-piperidols on their physiological activity we synthesized a new series of compounds of this type. Using the acid chlorides we esterified the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m. p. 107-108°) (I), the propionic ester of which is a powerful analgesic, widely used at the present time under the name of "promedol" [2].


(I)

In this manner we prepared the p-methoxyphenoxyacetic (II), p-ethoxyphenoxyacetic (III), α-phenoxypropionic (IV), α-phenoxyisobutyric (V), α-p-chlorophenoxyisobutyric (VI), p-nitrophenoxyacetic (VII), p-aminophenoxyacetic (VIII), diphenylacetic (IX), phenylpropiolic (X), pyromucic (XI) and β-phenylmercaptopropionic (XII) esters of the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol.

Based on the data of the pharmacological testing, made in the M. L. Mashkovskii laboratory, some of the indicated esters show appreciable local anesthetic action. Especially outstanding are the β-phenylmercaptopropionic (XII) and p-methoxyphenoxyacetic (II) esters, which are much more powerful than dikain** and at the same time are appreciably less toxic. The anesthetic activity of esters (II) and (XII) does not change after sterilization. The phenylpropiolic ester (X) proves to be a strong irritant. The degree of anesthetic activity, determined by the Regnier method, of some of the compounds prepared by us is shown in the table.

The chloride of β-phenylmercaptopropionic acid, used to synthesize ester (XII), was obtained from thiophenol and acrylonitrile in 75% yield by the scheme

$$C_6H_5SH + CH_2{=}CH{-}CN \longrightarrow C_6H_5SCH_2CH_2CN \xrightarrow[HCl]{H_2O}$$
$$\longrightarrow C_6H_5SCH_2CH_2COOH \xrightarrow{SOCl_2} C_6H_5SCH_2CH_2COCl.$$

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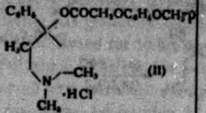
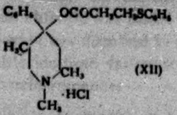
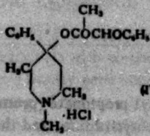
* Deceased.

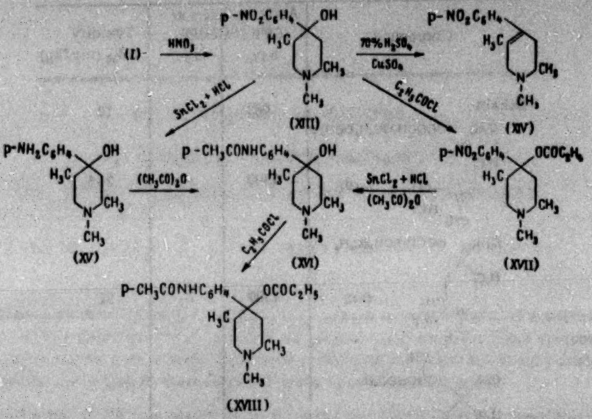
** Transliteration of Russian, commonly known in USA as pontocain hydrochloride or tetracaine hydrochloride — Publisher's note.

Compound	Activity index at concentration		Toxicity LD$_{50}$ (mg/kg)
	0.1%	0.5%	
Dikain	683	—	10
 (II)	1300	—	24.5
 (XII)	1300	—	31
 (IV)	—	952	—

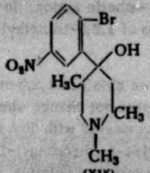
Earlier we had prepared a number of 1,2,5-trimethyl-4-phenyl-4-piperidols [3], containing different substituents in the phenyl radical. The physiological activity of the esters of these substituted 4-phenyl-4-piperidols is frequently quite different from the activity of the analogous esters of 1,2,5-trimethyl-4-phenyl-4-piperidol itself. For example, the propionate of 1,2,5-trimethyl-4-(2'-methoxy-5'-bromophenyl)-4-piperidol, being an analog of promedol, is devoid of analgesic properties, but does show local anesthetic action. In this study we made an attempt to introduce the nitro and amino groups into the aromatic nucleus of 1,2,5-trimethyl-4-phenyl-4-piperidol.

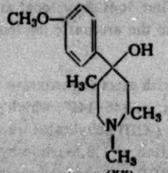
By directly treating the γ-isomer (I) at 50-60° with nitrating mixture we obtained 1,2,5-trimethyl-4-p-nitrophenyl-4-piperidol (XIII) in 40% yield and with m. p. 146-149°, which does not change when heated with 10% alcoholic potassium hydroxide solution. Piperidol (XIII) dehydrates when treated with 70% sulfuric acid in the presence of copper sulfate with the apparent formation of 1,2,5-trimethyl-4-p-nitrophenyl-1,2,3,6-tetrahydropyridine (XIV). Later the nitro group in piperidol (XIII) was reduced using stannous chloride, and here 1,2,5-trimethyl-4-p-aminophenyl-4-piperidol (XV) was obtained in 83% yield. An attempt to replace the amino group in piperidol (XV) by hydroxyl proved unsuccessful. Decomposition of the diazo compound, obtained by treating piperidol (XV) in acid solution with sodium nitrite, proceeds with the copious evolution of nitrogen and is accompanied by tar formation. Similar tar formation is observed when the diazo compound, obtained from piperidol (XV), is coupled with β-naphthol. The bright red solution that is obtained here rapidly darkens, and the desired azo compound cannot be isolated (see diagram on following page).

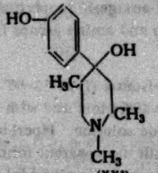
The reaction of acetic anhydride with 1,2,5-trimethyl-4-p-aminophenyl-4-piperidol (XV) yields 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol (XVI), which was also obtained by a different route. Reaction of 1,2,5-trimethyl-4-p-nitrophenyl-4-piperidol (XIII) with propionyl chloride in benzene gave the propionic ester (XVII) of this piperidol. Reduction of the nitro group in the last compound with stannous chloride and concentrated hydrochloric acid in alcohol solution is accompanied by simultaneous saponification of the ester grouping. The resulting piperidol (XV) was not isolated in this case, but instead was immediately treated with acetic anhydride, and this gave the above described 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol (XVI). Esterification of piperidol (XVI) with propionyl chloride in benzene gave the propionic ester (XVIII) of 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol. In contrast to promedol, propionic ester (XVII), containing a nitro group in the phenyl radical, as well as propionate (XVIII), containing an acetamido group in the phenyl radical, do not show analgesic activity.

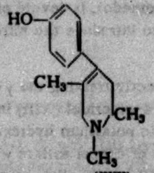


The direct nitration of 1,2,5-trimethyl-4-phenyl-4-piperidyl propionate (promedol) is accompanied by strong tarring of the substance. Reaction of p-bromonitrobenzene with butyllithium, and this with 1,2,5-trimethyl-4-piperidone, gave 1,2,5-trimethyl-4-(2'-bromo-5'-nitrophenyl)-4-piperidol (XIX) in very low yield (about 1%). We also attempted to prepare 1,2,5-trimethyl-4-p-hydroxyphenyl-4-piperdol (XXI) by heating 1,2,5-trimethyl-4-p-methoxyphenyl-4-piperidol (XX) with concentrated hydrobromic acid. However, this reaction is accompanied by dehydration, and instead of piperidol (XXI), we isolated 1,2,5-trimethyl-4-p-hydroxyphenyl-1,2,3,6-tetrahydropyridine (XXII).


(XIX)


(XX)


(XXI)


(XXII)

The complete results of the pharmacological testing of the obtained compounds will be published in a separate communication.

EXPERIMENTAL

For the esterifications we used γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m. p. 107-108°), described in previous communications [1,4].

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-methoxyphenoxyacetate (II). A mixture of 7.9 g of (I), 10 ml of dry benzene and 14 g of freshly distilled p-methoxyphenoxyacetyl chloride (b. p. 136-138° at 8 mm) was heated for 4 hrs on the water bath. The obtained crystalline precipitate was filtered the next day and repeatedly washed with benzene. After drying we obtained 10.7 g of the hydrochloride of ester (II), which after two recrystallizations from acetone melted at 189-190°.

Found %: N 3.44, 3.61. $C_{23}H_{30}O_4NCl$. Calculated %: N 3.50.

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-ethoxyphenoxyacetate (III). For reaction we took 6 g of (I), 7 ml of dry benzene and 12 g of freshly distilled p-ethoxyphenoxyacetyl chloride (b. p. 148-149° at 9 mm). The reaction was run in the same manner as above. After two recrystallizations from acetone we obtained 3.4 g of the hydrochloride of ester (III) with m. p. 195-196°.

Found %: N 3.33, 3.41. $C_{24}H_{32}O_4NCl$. Calculated %: N 3.22.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-phenoxypropionate (IV). To a solution of 3 g of (I) in 5 ml of benzene with cooling and stirring was gradually added 6 g of freshly distilled α-phenoxypropionyl chloride (b. p. 124° at 3 mm). The mixture was heated for 10 hrs on the water bath. The benzene was vacuum-distilled from the extremely dark reaction mixture. The residue was dissolved in water and treated with saturated soda solution. The organic bases that separated here were extracted with ether, dried over sodium sulfate, and fractionally distilled in vacuo. We obtained two fractions: 1st fraction, b. p. 113-120° at 2.5 mm, 0.4 g; 2nd fraction, 160-182° at 2.5 mm, 2.1 g. Dry hydrogen chloride was passed into an ether solution of the 2nd fraction. The resulting precipitate of ester (IV) hydrochloride was dissolved in acetone and again precipitated with ether. An attempt to recrystallize ester (IV) hydrochloride from various solvents proved unsuccessful. The substance represents colorless crystals, melting at 90° with effervescence.

Found %: N 3.80, 3.82. $C_{23}H_{30}O_3NCl$. Calculated %: N 3.47.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-phenoxyisobutyrate (V). This ester could not be obtained by the direct esterification of piperidol (I) with α-phenoxyisobutyric chloride, using the technique of the preceding experiments. The esterification hardly goes under mild conditions, while long heating at elevated temperature (111-120°) causes pronounced tarring of the reaction mass. A similar situation was also observed by us earlier when we attempted to esterify piperidol (I) with acids having a branched carbon chain. Thus, for example, we were unable to obtain the trimethylacetic and isobutyric esters by this technique. Esterification is also difficult in the case of reacting piperidol (I) with isovaleryl chloride. The isobutyric and isovaleric esters were obtained [1] through the lithium alcoholate of piperidol (I). This method was also used to obtain the ester described below (V).

The lithium alcoholate of 1,2,5-trimethyl-4-phenyl-4-piperidol was prepared from 1 g of lithium, 15.3 g of bromobenzene and 8.5 g of 1,2,5-trimethyl-4-piperidone in 200 ml of absolute ether. Then to the reaction mass with vigorous stirring was added 24 g of α-phenoxyisobutyryl chloride (b. p. 101° at 8 mm). The mixture was heated at ether boil for 4 hrs and then 50 ml of water was added, the ether layer separated, and the lower water layer treated with soda. The organic bases that separated here were extracted with ether, dried, and vacuum-distilled. The following fractions were obtained: 1st fraction, b. p. 143-175° at 2.5 mm, 8 g; 2nd fraction, 175-186° at 2.5 mm, 29 g. From 0.7 g of the 2nd fraction we obtained 0.8 g of the picrate of ester (V) with m. p. 190-191° (from alcohol).

Found %: N 9.27, 9.51. $C_{30}H_{34}O_{10}N_4$. Calculated %: N 9.18.

The passage of hydrogen chloride into an ether solution of the 2nd fraction gave the hydrochloride as a viscous precipitate, which could not be made to crystallize.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-p-chlorophenoxyisobutyrate (VI). A mixture of 8 g of (I), 8 ml of dry benzene and 17.5 g of α-p-chlorophenoxyisobutyryl chloride (b. p. 130-131° at 10 mm) was heated for 4 hrs on the water bath. The benzene was vacuum-distilled from the dark reaction mass, and the residue was treated with soda to give the free organic bases. Vacuum-distillation of the bases gave a fraction with b. p. 190-230° at 2 mm (2.7 g), from which the picrate of ester (VI) with m. p. 150-152° (from alcohol) was isolated.

Found %: N 9.38, 9.15. $C_{30}H_{33}O_{10}N_4Cl$. Calculated %: N 8.68.

The hydrochloride of this ester was obtained as a noncrystallizing oil.

1,2,5-Trimethyl-4-phenyl-4-piperidol p-nitrophenoxyacetate (VII). A mixture of 10 g of (I), 15 ml of dry benzene, 0.1 g of magnesium and 21.1 g of p-nitrophenoxyacetyl chloride (m. p. 84-87.5°) was heated for 8 hrs at 70-80°. The next day the obtained precipitate was filtered and washed with acetone. We obtained 3.8 g of the hydrochloride of ester (VII), which after two recrystallizations from acetone melted at 186-188°.

Found %: N 6.07, 6.28; C 60.36, 60.79; H 5.81, 5.91. $C_{22}H_{27}O_5N_2Cl$. Calculated %: N 6.44; C 60.75; H 5.98.

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-aminophenoxyacetate (VIII). A solution of 12 g of stannous chloride in 15 ml of alcohol and 15 ml of concentrated hydrochloric acid was gradually added to a solution of 3 g of of ester (VII) hydrochloride in 50 ml of anhydrous ethanol at 50°. The mixture was heated on the water bath at 80° for 5 hrs. The alcohol was distilled under slight vacuum, and the residue was dissolved in water and treated with soda. The obtained oily layer of organic bases was extracted with ether, the ether solution dried, and then dry hydrogen chloride was passed into it. The obtained precipitate was recrystallized from acetone to give 0.4 g of ester (VIII) dihydrochloride with m. p. 155-156°.

Found %: N 6.60, 6.32. $C_{22}H_{30}O_3N_2Cl_2$. Calculated %: N 6.35.

1,2,5-Trimethyl-4-phenyl-4-piperidyl diphenylacetate (IX). A mixture of 3 g of (I), 5 ml of benzene and 14 g of diphenylacetyl chloride (b. p. 115-118° at 2.5 mm) was heated for 5 hrs at 70-80°. The product was diluted with absolute ether, the separated oil repeatedly washed with ether, and then dissolved in water. The aqueous solution was washed with ether, treated with dilute ammonia solution, the organic bases extracted with ether, the ether solution dried, and then treated with dry hydrogen chloride. The obtained crystals were recrystallized from acetone to give 2 g of ester (IX) hydrochloride with m. p. 194-195°.

Found %: N 2.99, 3.18. $C_{28}H_{32}O_2NCl$. Calculated %: N 3.11.

1,2,5-Trimethyl-4-phenyl-4-piperidyl phenylpropiolate (X). For reaction we took 3 g of (I), 4 ml of benzene and 4 g of phenylpropioloyl chloride (b. p. 111-113° at 15 mm). Much evolution of heat was observed during the addition of the chloride. The reaction mass was cooled in ice water, the voluminous crystalline precipitate filtered, washed on the filter with benzene, and recrystallized from acetone. We obtained 2.3 g of ester (X) hydrochloride with m. p. 169-170°.

Found %: N 3.41, 3.41. $C_{23}H_{26}O_2NCl$. Calculated %: N 3.65.

1,2,5-Trimethyl-4-phenyl-4-piperidyl pyromucate (XI). A mixture of 5 g of (I), 7.5 ml of benzene and 7.5 g of pyromucyl (2-furoyl) chloride (b. p. 72-73° at 18 mm) was heated at 70-80° for 3 hrs. After recrystallization from acetone, the obtained precipitate (4.2 g) of ester (XI) hydrochloride melted at 206-207°.

Found %: N 3.87, 4.20. $C_{19}H_{24}O_3NCl$. Calculated %: N 4.00.

The mother liquor from the above precipitate (4.2 g) was treated in conventional manner to give 3.4 g of the free ester (XI) with m. p. 92-94° (from benzine*).

Found %: N 4.59, 4.63. $C_{19}H_{23}O_3N$. Calculated %: N 4.47.

1,2,5-Trimethyl-4-phenyl-4-piperidyl β-phenylmercaptopropionate (XII). a) β-Phenylmercaptopropionyl chloride. To 20 g of thiophenol was added two drops of a saturated alcoholic solution of sodium ethylate, and then 16 g of acrylonitrile was gradually added with cooling. The mixture was heated for 8 hrs at 50° and for 2 hrs in a boiling water bath. Distillation gave 27 g of β-phenylmercaptopropionitrile with b. p. 111-112° at 3 mm, which was heated for 4 hrs on the water bath (80-90°) with 35 g of concentrated hydrochloric acid under vigorous stirring. The mixture after cooling was treated with 50 ml of water, and the obtained precipitate was extracted with ether. We obtained 30 g of β-phenylmercaptopropionic acid with m. p. 58-59° (from water), which was treated with 50 ml of thionyl chloride, and after conventional treatment we obtained 27.5 g of β-phenylmercaptopropionyl chloride with b. p. 139° at 4 mm.

b) 1,2,5-Trimethyl-4-phenyl-4-piperidyl β-phenylmercaptopropionate (XII). A mixture of 7 g of (I), 10 ml of dry benzene and 17 g of β-phenylmercaptopropionyl chloride was heated for 10 hrs at vigorous benzene reflux. The benzene was vacuum-distilled, and the residue was treated with 30 ml of water and 30 ml of ether. A dark viscous oil, insoluble in both water and ether, settled on the bottom of the flask, which was separated and treated with dilute ammonia solution in the presence of ether. The ether extract of the bases was dried over sodium sulfate and then treated with hydrogen chloride to give an oil, readily soluble in acetone and benzene. Recrystallization from benzene gave 0.5 g of ester (XII) hydrochloride with m. p. 158-161°.

Found %: N 3.55, 3.53. $C_{23}H_{30}O_2NSCl$. Calculated %: N 3.33.

1,2,5-Trimethyl-4-p-nitrophenyl-4-piperidol (XIII). 3 g of (I) was added in small portions to a mixture of 1.6 ml of nitric acid (d 1.36) and 2 ml of sulfuric acid (d 1.84). After heating on the water bath for 45 min at

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* As in original — Publisher's note.

60° the reaction mass was poured into 50 ml of cold water. The aqueous solution was treated with soda, and the organic bases were extracted with ether and dried over sodium sulfate. Removal of the ether by distillation gave 3.2 g of residue, which recrystallized from benzine* gave 1 g of (XIII) with m. p. 146-149°.

Found %: N 10.65, 10.66. $C_{14}H_{20}O_3N_2$. Calculated %: N 10.60.

1,2,5-Trimethyl-4-p-nitrophenyl-1,2,3,6-tetrahydropyridine (XIV). A mixture of 2 g of (XIII), 3.5 g of 70% sulfuric acid and 0.5 g of fused copper sulfate was heated for 4 hrs in a boiling water bath. Treatment with water and extraction with ether gave 1.5 g of (XIV) as a mobile liquid, from which the picrate with m. p. 155-157° (from alcohol) was obtained.

Found %: N 14.92, 14.84. $C_{20}H_{21}O_9N_5$. Calculated %: N 14.72.

1,2,5-Trimethyl-4-p-aminophenyl-4-piperidol (XV). A solution of 10 g of stannous chloride in 15 ml of alcohol and 15 ml of concentrated hydrochloric acid was gradually added to a solution of 2.8 g of (XIII) in 50 ml of anhydrous alcohol heated to 50°. After heating for 6 hrs on the water bath the solvent was distilled off, and the residue was dissolved in water and treated with potassium hydroxide. The free base that separated here was extracted with ether, dried over sodium sulfate, and then fractionally distilled to give 2 g of (XV) with m. p. 139-140° (from benzine).

Found %: N 11.72, 11.80. $C_{14}H_{22}ON_2$. Calculated %: N 11.53.

1,2,5-Trimethyl-4-p-acetamidophenyl-4-piperidol (XVI). a) A solution of 0.2 g of (XV) in 20 ml of 5% hydrochloric acid was treated at 50° with 1 ml of acetic anhydride. The product was treated with saturated soda solution, extracted with ether, and the ether partially evaporated to give 0.15 ml of (XVI) as crystals with m. p. 231-233°.

Found %: N 10.18, 10.03. $C_{16}H_{24}O_2N_2$. Calculated %: N 10.01.

b) 3 g of the propionate (XVII) hydrochloride was reduced with stannous chloride (12 g) in an alcoholic solution of concentrated hydrochloric acid (alcohol 65 ml, acid 15 ml) at the boil for 5 hrs. We obtained 2.7 g of reduction product, which without purification was acetylated with acetic anhydride (1.6 g) by the above-described procedure. We obtained 1.5 g of (XVI) with m. p. 231-233°, failing to depress the melting point when mixed with the above-obtained specimen.

1,2,5-Trimethyl-4- p-nitrophenyl-4-piperidyl propionate (XVII). A mixture of 3 g of (XIII), 5 ml of dry benzene and 3 ml of propionyl chloride was heated at benzene boil for 3 hrs. The flask contents crystallized on cooling. The crystals were separated, washed with benzene, and recrystallized twice from acetone. We obtained 1.8 g of propionate (XVII) hydrochloride with m. p. 244-245.5°.

Found %: N 7.90, 7.63. $C_{17}H_{25}O_4N_2Cl$. Calculated %: N 7.85.

1,2,5-Trimethyl-4-p-acetamidophenyl-4-piperidyl propionate (XVIII). A mixture of 1.5 g of (XVI), 6 ml of dry benzene and 2 ml of propionyl chloride was heated for 4 hrs at benzene reflux. The benzene together with excess propionyl chloride was decanted, while the residual oil was dried in a vacuum-desiccator and then dissolved in acetone. Treatment of the acetone solution with absolute ether gave colorless crystals (0.9 g) of propionate (XVIII) hydrochloride, melting at 70° (with decomp.).

Found %: N 7.72, 7.46. $C_{19}H_{29}O_3N_2Cl$. Calculated %: N 7.59.

1,2,5-Trimethyl-4-(2'-bromo-5'-nitrophenyl)-4-piperidol (XIX). To the butyllithium, obtained from 7.2 g of lithium and 50 g of butyl bromide in 300 ml of absolute ether, was added with cooling in ice water a solution of 52.5 g of p-bromonitrobenzene (m. p. 125-126°) in 200 ml of ether. After vigorous stirring for 1 hr, 36 g of 1,2,5-trimethyl-4-piperidone was added in drops. The product was treated with water (50 ml) and 18% hydrochloric acid (170 ml). The water layer was treated with potassium hydroxide, and the bases that separated here were extracted with ether, dried, and vacuum-distilled. We obtained 25.6 g of 1,2,5-trimethyl-4-piperidone and 1 g of a fraction with b. p. 160° at 3 mm, which crystallized in the receiver. Recrystallization from bezine gave 0.3 g of (XIX) as orange crystals with m. p. 192-195°.

Found %: N 8.24, 8.41. $C_{14}H_{19}O_3N_2Br$. Calculated %: N 8.17.

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* As in original – Publisher's note.

1,2,5-Trimethyl-4-p-hydroxyphenyl-1,2,3,6-tetrahydropyridine (XXII). A mixture of 2 g of (XX) (m. p. 99-100°) [3], 15 ml of concentrated hydrobromic acid and 20 ml of glacial acetic acid was heated in a boiling water bath for 5 hrs. The acids were vacuum-distilled, while the residue was dissolved in water and treated with sodium hydroxide. The ether extract of organic bases was dried over fused sodium sulfate. Removal of the ether by distillation left 0.5 g of mobile liquid, from which the picrate of (XXII) with m. p. 134-136° (from alcohol) was obtained.

Found %: N 12.70, 12.46. $C_{20}H_{22}O_8N_4$. Calculated %: N 12.56.

SUMMARY

For the purpose of pharmacological testing and to study the relationship between the structure and physiological action of esters of 4-aryl-4-piperidols we synthesized a new series of compounds of this type. Two of the synthesized esters, namely the β-phenylmercaptopropionic and p-methoxyphenoxyacetic esters of 1,2,5-trimethyl-4-phenyl-4-piperidol, show a high anesthetic activity and a comparatively low toxicity.

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Received April 1, 1957

Institute of Fine Chemical Technology, Moscow

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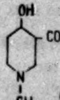
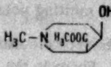
SYNTHESIS OF N-METHYL-3-CARBOMETHOXY-4-HYDROXYPIPERIDINES AND A STUDY OF THEIR STERIC STRUCTURES

M. E. Maurit and N. A. Preobrazhenskii

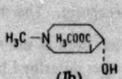
In our paper on the synthesis of arecoline and its homologs [1] we described the preparation of this alkaloid from methyl acrylate and from acrylonitrile. The intermediate in this synthesis is N-methyl-3-carbomethoxy-4-hydroxypiperidine (I). As can be seen from the given formula, piperidol (I) has two asymmetric carbon atoms, and according to theory it is possible for two racemic stereoisomers (Ia) (cis-3:4) and (Ib) (trans-3:4) to exist.



(I)



(Ia)



(Ib)

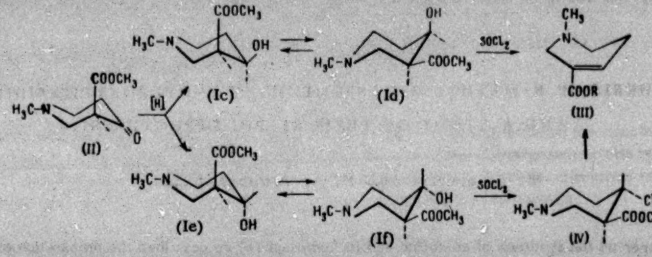
In this paper we investigated various methods for the reduction of N-methyl-3-carbomethoxy-4-piperidone (II) to the corresponding piperidol (Ia, Ib), the separation of the isomeric piperidols, and the conditions of their dehydration.

The catalytic reduction of ketone (II) using skeletal nickel catalyst gave chiefly one isomer with m. p. 86-87°, the hydrobromide of which had m. p. 144.5-145.5°. Reduction using sodium amalgam gave a mixture of piperidols with m. p. 65-68°, which was separated by recrystallizing their hydrobromides from either anhydrous ethyl or isopropyl alcohol. Here we isolated a piperidol hydrobromide with m. p. 181-182° (30%), from which a base with m. p. 96-97° was obtained,and a second hydrobromide with m. p. 142-143° (19%), corresponding to the base with m. p. 86-87°.

Electrochemical reduction at a lead cathode in alkaline medium gave a mixture of hydrochlorides of the isomeric N-methyl-4-hydroxyhexahydronicotinic acids, which by conventional esterification was converted into the methyl esters of the corresponding bases. From this mixture of piperidols, having m. p. 72-77°, we also obtained two hydrobromides, one with m. p. 182-182.5° (12%) and the other with m. p. 143-144° (18.8%). The mixed melting point of the piperidol hydrobromides with m. p. 144.5-145.5° and 182-182.5° is 130-152°, and that of the free bases with m. p. 86-87° and 96-97° is 67-70°.

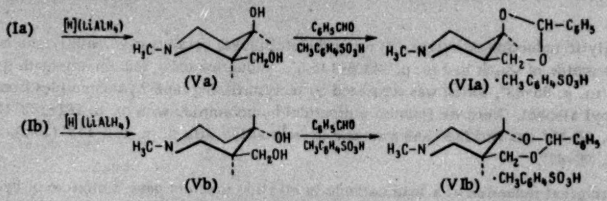
When the reaction of the isomeric N-methyl-3-carbomethoxy-4-hydroxypiperidines with thionyl chloride was investigated,we found that the piperidol with m. p. 86-87° is easily dehydrated to yield arecoline (III, R = = CH_3), whereas the piperidol with m. p. 96-97° is converted to N-methyl-3-carbomethoxy-4-chloropiperidine (IV). Chloro derivative (IV), having the same configuration as the starting hydroxy compound (Ib), apparently suffers Walden inversion when treated with alkali and cleaves a molecule of hydrogen chloride, in which connection the ester group is saponified at the same time to yield arecaidine (III, R = H), which we isolated and identified as the hydrochloride.

Consequently, based on the differences between the piperidol with m. p. 86-87° and the piperidol with m. p. 96-97, the N-methyl-3-carbomethoxy-4-hydroxypiperidines show cis (Ia)-trans (Ib) isomerism. However, the answer to the question as to which configuration corresponds to the hydroxy derivative with m. p. 86-87° or with m. p. 96-97° presents greater difficulties. Since water is usually cleaved more easily from a cis-isomer than from the trans-isomer, and since compounds of the cis-series have lower melting and boiling points than do trans-compounds, then the piperidol with m. p. 86-87° must be the cis-isomer (Ia), and the piperidol with m. p. 96-97° the trans-isomer (Ib).


COOCH$_3$
H$_3$C-N
OH
(Ic)
OH
H$_3$C-N
COOCH$_3$
(Id)
SOCl$_2$
CH$_3$
N
COOR
(III)
COOCH$_3$
H$_3$C-N
O
(II)
[H]
COOCH$_3$
H$_3$C-N
(Ie)
OH
H$_3$C-N
OH
COOCH$_3$
(If)
SOCl$_2$
H$_3$C-N
Cl
COOCH$_3$
(IV)

To support this position we adopted the method used by G. Fodor to establish spatial configuration in the series of tropane alkaloids [2]. Both piperidol isomers were reduced with aluminum lithium hydride to the corresponding diols (Va and Vb), which when reacted with benzaldehyde in the presence of toluenesulfonic acid both gave O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ol toluenesulfonates (VIa and VIb) with m. p. 173-174° and 200-202°, respectively. The mixed melting point of these salts was 168-170°.

As a result, it proved that both of the piperidol stereoisomers can give benzylidene derivatives, in contrast to the cis- and trans- derivatives described by G. Fodor in the tropane series. This tendency to form cyclic acetals can be explained on the basis of the conformation of both the cis-3:4 (Ic, Id) and trans-3:4 (Ie, If) N-methyl-3-carbomethoxy-4-hydroxypiperidols. From the presented formulas it can be seen that for both the cis- and trans-isomers it is possible to have such structure conformations as to put the hydroxyl groups sufficiently close to each other to permit forming the six-membered ring of the benzylidene derivative.


(Ia)
[H](LiAlH$_4$)
OH
H$_3$C-N
CH$_2$OH
(Va)
C$_6$H$_5$CHO
CH$_3$C$_6$H$_4$SO$_3$H
O
CH-C$_6$H$_5$
H$_3$C-N
CH$_2$-O
(VIa) ·CH$_3$C$_6$H$_4$SO$_3$H
(Ib)
[H] (LiAlH$_4$)
OH
H$_3$C-N
CH$_2$OH
(Vb)
C$_6$H$_5$CHO
CH$_3$C$_6$H$_4$SO$_3$H
O-CH-C$_6$H$_5$
H$_3$C-N
CH$_2$-O
(VIb) ·CH$_3$C$_6$H$_4$SO$_3$H

EXPERIMENTAL

1. Methyl esters of isomeric N-methyl-4-hydroxypiperidine-3-carboxylic acids. a) Catalytic reduction. The reduction of N-methyl-3-carbomethoxy-4-piperidone (II) in the presence of skeletal nickel catalyst was run in the same manner as described in the previous paper [1]. We obtained 34.8 g of piperidol (Ia) from 51.3 g of technical ketone (II) (67% yield, based on ketone). B. p. 114-118° at 8 mm. The free piperidol base (Ia) was recrystallized from anhydrous ethyl alcohol. M. p. 86-87°.

Hydrobromide of piperidol (Ia). A solution of 8.66 g of the free piperidol base (Ia) in 20 ml of anhydrous alcohol was treated at 0° with an alcoholic solution of hydrogen bromide (until acid to Congo). The mixture was cooled to −10° and the obtained crystals were filtered. M. p. 142-144°. Yield 11.7 g (92.1%); after recrystallization from anhydrous ethyl alcohol (1 : 3) the compound melted at 144.5-145.5°.

Found %: C 37.92, 37.97; H 6.15, 6.20; N 5.37, 5.31; Br 31.60. $C_8H_{15}O_3N \cdot HBr$. Calculated %: C 37.83; H 6.35; N 5.51; Br 31.45.

Free base N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ia) from the hydrobromide with m. p. 144.5-145.5°. A solution of 9 g of piperidol (Ia) hydrobromide with m. p. 144.5-145.5° in 6 ml of water was made alkaline with ammonia solution. The free base was extracted with chloroform. Yield 6 g (97.8%). M. p. 86-87°.

Found %: C 55.42; H 8.45; N 7.92, 8.01. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

b) Electrochemical reduction at lead cathode in alkaline medium. A water solution of the sodio derivative of N-methyl-3-carbomethoxy-4-piperidone (II), obtained from the cyclization of 46.5 g of β,β'-dicarbomethoxydiethylmethylamine, was placed in a porous beaker and subjected to reduction at a lead cathode with a current strength of 7-8 amp, a potential difference of 5-6 v and a temperature of 18-20° for 10-12 hrs. Both the cyclization and the reduction were run by the method described in the previous paper [1]. The solution obtained after reduction was acidified with hydrochloric acid and then evaporated in vacuo. The hydrochlorides of the N-methyl-4-hydroxyhexahydronicotinic acids were extracted from the dry residue with hot methyl alcohol (3 times with 70 ml portions). Then the extract was treated with 10 ml of concentrated sulfuric acid and the whole heated at the boil for 5 hrs, after which the excess alcohol was distilled off, the residue neutralized with saturated potash solution (to phenolphthalein) with efficient cooling, and the piperidols (Ia and Ib) extracted with chloroform (3 times with 30 ml portions). The solvent was distilled off, and the residue was vacuum-distilled. Yield of N-methyl-3-carbomethoxy-4-hydroxypiperidines (Ia and Ib) 21.5 g (54.2%), based on β,β'-dicarbomethoxydiethylmethylamine. B. p. 110-122° at 8 mm. The piperidols were recrystallized from anhydrous ethyl alcohol. M. p. 72-77°.

Found %: C 55.27; H 8.50; N 7.97. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

The mixed melting point of piperidol (Ia) with m. p. 86-87° (from catalytic reduction) and mixture (Ia and Ib) of piperidols with m. p. 72-77° (from electrochemical reduction) was 72-80°.

Hydrobromides of piperidols (Ib and Ia). The mixed piperidols (21.5 g) with m. p. 72-77°, obtained from electrochemical reduction, were converted to the hydrobromides in the same manner as described above for the free piperidol base (I) obtained after catalytic reduction. The yield of mixed N-methyl-3-carbomethoxy-4-hydroxypiperidine hydrobromides was 30.8 g (97.6%). M. p. 128-135°.

After 1 recrystallization from 15 volumes of anhydrous alcohol and 2 recrystallizations from 20 volumes we obtained 3.7 g of piperidol (Ib) hydrobromide (12% of the total amount of hydrobromides). M. p. 182-182.5°.

Found %: C 37.64; H 6.45; N 5.32, 5.48; Br 31.36. $C_8H_{15}O_3N \cdot HBr$. Calculated %: C 37.83; H 6.35; N 5.51; Br 31.45.

The mother liquors from the recrystallizations were distilled to remove solvent and the residual hydrobromide was recrystallized from anhydrous isopropyl alcohol (1:1). The yield of piperidol (Ia) hydrobromide with m. p. 143-144.5° was 8 g (18.8% of the total amount of hydrobromides). The mixed melting point of the piperidol hydrobromides with m. p. 144.5-145.5° (from catalytic reduction) and with m. p. 182-182.5° (from electrochemical reduction) was 130-152°.

Free base N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ib) from piperidol (Ib) hydrobromide with m. p. 182-182.5°. From 7.6 g of piperidol (Ib) hydrobromide with m. p. 182-182.5° we isolated 4.94 g (95.4%) of free piperidol base (Ib), which was recrystallized from anhydrous alcohol. M. p. 96.5-97.5°.

Found %: C 55.65, 55.37; H 8.57, 8.57; N 8.32, 8.02. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

The mixed melting point of the piperidols with m. p. 86-87° and with m. p. 96.5-97.5° was 67-70°.

Reduction with sodium amalgam. To a solution of 17 g of N-methyl-3-carbomethoxy-4-piperidone hydrochloride (II · HCl) in 170 ml of water and 10 ml of concentrated hydrochloric acid was gradually added with vigorous stirring, at −2 to 0°, 930 g of 5% sodium amalgam (in portions of 19 g every 5-10 min). The reaction solution was maintained constantly acid by the addition of 200 ml of concentrated hydrochloric acid. When reduction was complete, which was established by testing with ferric chloride, the settled solution was decanted from the mercury, made alkaline with saturated potash solution (to phenolphthalein), and the free piperidols (Ia and Ib) extracted with chloroform (4 times with 40 ml portions). The solvent was distilled off, and the residue was vacuum-distilled. The yield of N-methyl-3-carbomethoxy-4-hydroxypiperidines (Ia and Ib) was 8.8 g (62.1%, based on ketone hydrochloride). B. p. 110-117° at 7 mm. The mixed piperidols were recrystallized from alcohol. M. p. 65-68°.

Hydrobromides of piperidols (Ia and Ib). From 7.5 g of mixed piperidols with m. p. 65-68°, obtained from reduction with sodium amalgam, we isolated 3.3 g of piperidol (Ib) hydrobromide with m. p. 181-182° (30%, based on the free base) and 2.1 g of piperidol (Ia) hydrobromide with m. p. 142-143° (19%). From the first hydrobromide we obtained the free piperidol (Ib) with m. p. 96-97°, and from the second – the free base (Ia) with m. p. 86-87°.

2. Reaction of thionyl chloride with isomeric piperidols (Ia and Ib). a) Free arecoline (III, R = CH_3). A solution of 3 g of free piperidol (Ia) with m. p. 86-87° in 15 ml of dry benzene was treated with 6 ml of thionyl chloride under cooling. After standing for 1 hr at room temperature the reaction mass was heated at reflux for 3 hrs, then the excess thionyl chloride and solvent were removed in vacuo, the residue dissolved in 5 ml of water, the solution made alkaline with aqueous ammonia, and the free arecoline extracted with ether (4 times with 5 ml portions). The extract was dried over sodium sulfate, the solvent distilled off, and the residue vacuum-distilled. The yield of arecoline as the free base was 1.7 g (63.2%, based on piperidol Ia).

B. p. 92-93° at 7 mm; $n^{20}D$ 1.4302, d^{20}_4 1.0495, MR_D 42.06. $C_8H_{13}O_2N$. Calculated 42.07.

Arecoline hydrobromide melts at 169-170°. Its mixture with the hydrobromide of the natural alkaloid (m. p. 169-170.5°) fails to show a melting point depression.

b) N-Methyl-3-carbomethoxy-4-chloropiperidine (IV). A solution of 2 g of free piperidol (Ib) with m. p. 96.5-97.5° (isolated from the hydrobromide with m. p. 182-182.5°) in 20 ml of benzene was treated with 4 ml of thionyl chloride. The remainder of the process was run in the same manner as described above for the isomeric piperidol (Ia) with m. p. 86-87°. Removal of the ether by distillation left the technical N-methyl-3-carbomethoxy-4-chloropiperidine (IV). Yield 2.15 g (97.2%, based on free piperidol Ib). M. p. 160-162°.

Chloro derivative (IV) was recrystallized from anhydrous ethyl alcohol (1: 3). M. p. 161-162°.

Found %: C 50.32, 49.96; H 7.32, 7.26; N 7.17; Cl 18.41, 18.39. $C_8H_{14}O_2NCl$. Calculated %: C 50.16; H 7.38; N 7.31; Cl 18.50.

c) Arecaidine hydrochloride (III, R = H · HCl). A solution of 0.8 g of N-methyl-3-carbomethoxy-4-chloropiperidine (IV) in 5 ml of water was made alkaline with 30% sodium hydroxide solution. After standing for 3 hrs at room temperature the solution was acidified with hydrochloric acid (to Congo) and then evaporated in vacuo. Arecaidine hydrochloride was extracted from the dry residue with hot methyl alcohol. Removal of the solvent by distillation left 0.7 g of technical arecaidine hydrochloride (94.4%, based on the chloro derivative) with m. p. 245-248°. After recrystallization from a mixture of 10 ml of ethyl alcohol and 10 ml of methyl alcohol the arecaidine hydrochloride melted at 250.5-251°, and based on the physicochemical data, corresponds to the hydrochloride obtained from the natural alkaloid [3].

Found %: C 47.09; H 6.50; N 7.47, 7.61; Cl 20.41. $C_7H_{11}O_2N \cdot HCl$. Calculated %: C 47.34; H 6.81; N 7.88; Cl 19.96.

3. Isomeric N-methyl-3-hydroxymethyl-4-hydroxypiperidines (Va, Vb). a) A solution of 3 g of free base (Ia) with m. p. 86-87° in 100 ml of dry ether was added in 1 hr to an ether solution of aluminum lithium hydride (240 ml of solution containing 0.015 g of aluminum lithium hydride per ml) at −2 to 0°, after which the reaction mass was stirred at room temperature for 4 hrs. Then 7 ml of water was cautiously added with external cooling in ice, the mixture stirred for 1 hr at 18-20°, and the obtained precipitate filtered and washed with anhydrous methyl alcohol (3 times with 10 ml portions). The solvent was removed from the combined extracts by distillation, and the residue was vacuum-distilled. Yield 1.5 g (59.6%, based on free piperidol I); thick viscous oil, readily soluble in water and alcohol, and insoluble in ether, benzene and chloroform. B. p. 154-155° at 7 mm, $n^{20}D$ 1.5058.

Found %: C 58.18, 58.06; H 10.29, 10.55; N 9.32, 9.18. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

N-Methyl-3-hydroxymethyl-4-hydroxypiperidine hydrobromide (Va · HBr) was obtained as colorless crystals, readily soluble in water and hot alcohol, more difficultly soluble in cold alcohol, and insoluble in ether. M. p. 136-136.5°.

Found %: C 36.90, 37.24; H 7.14, 7.18; N 6.43, 6.06; Br 35.56, 35.46. $C_7H_{15}O_2N \cdot HBr$. Calculated %: C 37.18; H 7.12; N 6.20; Br 35.34.

b) From 2.4 g of free N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ib) with m. p. 95.5-96.5° we obtained in a similar manner 1.3 g (64.6%) of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Vb). Colorless viscous oil, readily soluble in water and alcohol, and insoluble in ether, chloroform and benzene. The compound crystallized on standing. B. p. 156-157° at 7 mm, $n^{20}D$ 1.5026; b. p. 67-68°.

Found %: C 58.09, 57.97; H 10.08, 10.29; N 9.42, 9.50. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

N-Methyl-3-hydroxymethyl-4-hydroxypiperidine hydrobromide (Vb · HBr) was obtained as colorless crystals, readily soluble in water and hot alcohol, more difficultly soluble in cold alcohol, and deliquescent in the air. M. p. 138-140° (softens at 75°).

Found %: C 37.47, 37.20; H 6.94, 7.20; N 6.14, 5.91; Br 34.80, 35.22. $C_7H_{15}O_2N \cdot HBr$. Calculated %: C 37.18; H 7.12; N 6.20; Br 35.34.

The mixed melting point of the diol hydrobromides (Va · HBr) with m. p. 136-136.5° and (Vb · HBr) with m. p. 138-140° was 118-120° (softens at 55°).

4. Isomeric O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ol toluenesulfonates (VIa and VIb). A mixture of 0.58 g of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Va), obtained from the free piperidol (Ia) with m. p. 86-87°, 6 ml of freshly distilled benzaldehyde and 0.83 g of toluenesulfonic acid was heated at 40 mm and a temperature of 85° for 5 hrs, and here some of the benzaldehyde distilled into the sulfuric acid. Since crystallization failed to occur on cooling, the excess benzaldehyde was vacuum-distilled at 10 mm and a bath temperature not exceeding 75°. The residue was treated with 2 ml of anhydrous alcohol and 10 ml of dry ether and the obtained crystals were filtered. The yield of O,O'-benzylidene toluenesulfonate derivative (VIa) was 1.5 g (92.6%). The toluenesulfonate was recrystallized from anhydrous alcohol. M. p. 173-174°.

Found %: C 62.35, 62.11; H 6.69, 6.37; N 3.51, 3.53. $C_{21}H_{27}O_5NS$. Calculated %: C 62.20; H 6.71; N 3.45.

b) A mixture of 0.43 g of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Vb), obtained from the free piperidol (Ib) with m. p. 96.5-97.5°, 5 ml of benzaldehyde and 0.62 g of toluenesulfonic acid was heated in vacuo at 85° and 40 mm for 5 hrs. The crystals obtained on cooling were filtered, washed with ether, and recrystallized from anhydrous alcohol. The yield of O,O'-benzylidene toluenesulfonate derivative was 1.1 g (91.6%). M. p. 200-202°.

Found %: C 62.34, 62.14; H 6.89, 6.37; N 3.49, 3.65. $C_{21}H_{27}O_5NS$. Calculated %: C 62.20; H 6.71; N 3.45.

The mixed melting point of the benzylidene toluenesulfonates (VIa) with m. p. 173-174° and (VIb) with m. p. 201-202° was 163-170° (softens at 155°).

SUMMARY

1. Depending on the reducing agent and reduction conditions, it was established that methyl esters of N-methyl-4-hydroxypiperidine-3-carboxylic acid are obtained with a variable relative amount of steric isomers.

2. Two isomers of N-methyl-3-carbomethoxy-4-hydroxypiperidine with m. p. 86-87° and 96.5-97.5° were isolated.

3. In studying the dehydration of the isomeric piperidols with thionyl chloride it was established that the piperidol with m. p. 86-87° gives the base arecoline, while the piperidol with m. p. 96.5-97.5° yields N-methyl-3-carbomethoxy-4-chloropiperidine.

4. The methyl esters of the isomeric N-methyl-3-carboxy-4-piperidols were reduced with aluminum lithium hydride and the obtained isomers of N-methyl-4-hydroxypiperidine were converted to the toluenesulfonates of the isomeric O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ols.

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Received April 1, 1957

Institute of Fine Chemical Technology, Moscow

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* Original Russian pagination. See C. B. translation.

CHEMISTRY OF HETEROCYCLES

XXXII. DI- AND POLYHALO DERIVATIVES OF 9-PHENYLACRIDINE WITH POSITIONS OF HALOGEN IN DIFFERENT BENZENE RINGS

M. E. Konshin and P. A. Petiunin

In previous communications* we described methods for the preparation of mono- and dihalo derivatives of 9-phenylacridine based on 2-aminotriphenylcarbinol and its N-acyl derivatives. Since 9-phenylacridine is a multinuclear heterocycle, then undoubtedly there is interest in utilizing this method to synthesize di- and polyhalo derivatives of 9-phenylacridine with the halogens located in different benzene rings. Another reason for doing this is that compounds of this type are not described in the literature.

The starting di- and polyhalo derivatives of 2-aminotriphenylcarbinol were obtained in satisfactory yields by reacting p-chlorophenylmagnesium bromide with the proper halogenated methyl anthranilate derivatives. The structure and properties of the compounds (I-V) obtained in this manner are given in the table. All of the synthesized compounds are crystalline and show weakly basic properties; they are insoluble in dilute mineral acids and concentrated hydrochloric acid. In addition, compounds (II-V), containing three or more halogen atoms, do not form picrates with picric acid. All of the indicated compounds dissolve in concentrated sulfuric acid with a permanent dark red color. Dilution of such solutions with water results in the separation of the starting halo derivatives of 2-aminotriphenylcarbinol in unchanged form.

It should be mentioned that the basic properties of the halo derivatives of 2-aminotriphenylcarbinol depend to a large extent on the positions of the halogens. The grestest influence is exerted by introducing halogen into the aniline moiety of 2-aminotriphenylcarbinol, and to a lesser degree when halogen is introduced into the other benzene rings.

When halo derivatives of 2-aminotriphenylcarbinol (I-V) are heated in nitrobenzene solution they are easily converted into halo derivatives of 9-phenylacridine with the halogens located in different benzene rings (VI-X). The latter are insoluble in dilute mineral acids. They readily dissolve in concentrated sulfuric acid with a yellow-green fluorescence. The basic properties of the acridine bases, the same as in the case of the halo derivatives of 2-aminotriphenylcarbinol, are materially influenced not only by the number of introducted halogen atoms, but also by their location. Thus, for example, compounds containing three halogens atoms in the molecule (VI, VII and IX), in contrast to the 2,4-dihalo derivatives of 9-phenylacridine, form picrates with picric acid. Polyhalo derivatives, containing 4 halogen atoms in the molecule (VIII and IX), do not form picrates. From the data given in the table it can be seen that the melting points of the halo derivatives of 9-phenylacridine increase uniformly with increase in the number of halogen atoms present.

EXPERIMENTAL

4', 4"-Dichloro-2-aminotriphenylcarbinol (I) was obtained by reacting 7.6 g (0.05 mole) of methyl anthranilate with 0.2 g-mole of p-chlorophenylmagnesium bromide. The compound is soluble in alcohol, benzine and acetic acid. It gives a red color with concentrated sulfuric acid. Yield 10.8 g (62.4%). Leaflets (from benzine).

Found %: N 3.84, 4.07; Cl 20.33, 20.52. $C_{19}H_{15}ONCl_2$. Calculated %: N 4.07; Cl 20.62.

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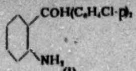
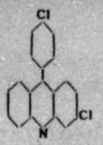
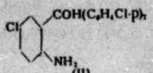
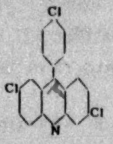
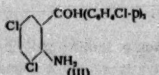
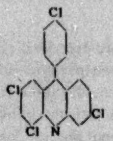
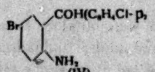
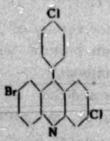
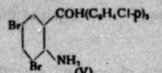
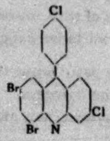
[*] J. Gen. Chem. 27, 475, 1558 (1957).

Halo derivatives of 2-aminotriphenylcarbinol	Melting point	Halo derivatives of 9-phenylacridine	Melting point
 (I)	116—117°	 (VI)	177—178°
 (II)	183—185	 (VII)	193—194
 (III)	148—149	 (VIII)	245—246
 (IV)	193 (decomp.)	 (IX)	205—207
 (V)	150—151.5	 (X)	254—255

The picrate was obtained as bright yellow leaflets with m. p. 200° (with decomp.).

4',4",5-Trichloro-2-aminotriphenylcarbinol (II) was obtained by reacting 4.6 g (0.025 g-mole) of methyl 5-chloroanthranilate with 0.1 g-mole of p-chlorophenylmagnesium bromide. The compound is readily soluble in alcohol and acetic acid, and insoluble in ether and benzene. Its solutions in concentrated sulfuric acid are colored red. Yield 9 g (95.8%).

Found %: N 3.64, 3.76. $C_{19}H_{14}ONCl_3$. Calculated %: N 3.74.

3,5,4',4"-Tetrachloro-2-aminotriphenylcarbinol (III). For reactions we took 8.5 g of methyl 3,5-dichloroanthranilate, 21.6 g of p-bromobenzene and 2.7 g of magnesium. Yield 7.5 g (47%). The compound is soluble in alcohol, ether, benzine and acetic acid. It gives a red-brown color with concentrated sulfuric acid. Crystals (from alcohol).

Found %: N 3.28, 3.52. $C_{19}H_{13}ONCl_4$. Calculated %: N 3.39.

5-Bromo-4',4"-dichloro-2-aminotriphenylcarbinol (IV). Starting substances: 9 g of methyl 5-bromoanthranilate, 22.9 g of p-bromobenzene and 2.88 g of magnesium. Yield 10.3 (62.6%). Readily soluble in acetic acid, more difficultly soluble in alcohol, and insoluble in ether. It gives a dark red color with concentrated sulfuric acid. Leaflets (from alcohol).

Found %: N 3.08, 3.11. $C_{19}H_{14}ONCl_2Br$. Calculated %: N 3.31.

3,5-Dibromo-4',4"-dichloro-2-aminotriphenylcarbinol (V). For reaction we took 19.1 g (0.1 mole) of p-bromochlorobenzene, 2.4 g (0.1 mole) of magnesium and 10.3 g (0.033 mole) of methyl 3,5-dibromoanthranilate. The compound is soluble in alcohol, ether, benzine and acetic acid. It gives a red-brown color with concentrated sulfuric acid. Yield 10 g (59.6%). Rhombic crystals (from benzine).

Found %: N 2.47, 2.64. $C_{19}H_{13}ONCl_2Br_2$. Calculated %: N 2.79.

3-Chloro-9-p-chlorophenylacridine (VI) was obtained by heating 1 g of (I) in 2 ml of nitrobenzene for 30 min. The precipitate obtained on cooling was filtered and recrystallized from alcohol. Yield 0.3 g (31.85%). The compound is soluble in alcohol and acetic acid, and readily dissolves in concentrated sulfuric acid with a yellow-green fluorescence. Bright yellow leaflets.

Found %: Cl 21.60, 21.63. $C_{19}H_{11}NCl_2$. Calculated %: Cl 21.89.

The picrate was obtained as yellow needles by mixing alcohol solutions of the compound and picric acid. M. p. 231-233°.

2,6-Dichloro-9-p-chlorophenylacridine (VII) was obtained in the same manner as the preceding from 1 g of (II) in 2 ml of nitrobenzene. Yield 0.3 g (31.6%). Soluble in alcohol and acetic acid, difficultly soluble in concentrated hydrochloric acid, and readily soluble in concentrated sulfuric acid. Its solutions in acids show a yellow-green fluorescence. Bright yellow clusters (from alcohol).

Found %: Cl 29.64, 29.70. $C_{19}H_{10}NCl_3$. Calculated %: Cl 29.68.

The picrate was obtained as yellow clusters (from alcohol) with m. p. 261-263°.

2,4,6-Trichloro-9-p-chlorophenylacridine (VIII). For reaction we took 1 g of (III) and 1 ml of nitrobenzene. Yield 0.54 g (56.7%). Soluble in benzene, acetone and chloroform, and insoluble in alcohol, ether, acetone and dilute mineral acids. Its solutions in concentrated sulfuric acid show a yellow-green fluorescence. Yellow crystals (from nitrobenzene).

Found %: N 3.91. $C_{19}H_9NCl_4$. Calculated %: N 3.56.

2-Bromo-6-chloro-9-p-chlorophenylacridine (IX). Reaction was run with 2.5 g of (IV) in 2.5 ml nitrobenzene The compound is soluble in acetic acid and alcohol, and insoluble in benzene, toluene, ether and dilute mineral acids. With concentrated sulfuric acid it forms solutions with a yellow-green fluorescence. Yield 1.5 g (63%). Golden yellow leaflets (from alcohol).

Found %: N 3.66, 3.72. $C_{19}H_{10}NCl_2Br$. Calculated %: N 3.47.

The picrate was obtained as orange crystals (from alcohol) with m. p. 268° (with decomp.).

2,4-Dibromo-6-chloro-9-p-chlorophenylacridine (X) was obtained from 2 g of (V) in 2 ml of nitrobenzene. Yield 1.2 g (62.5%). Soluble in toluene, chloroform and dioxane, and insoluble in alcohol, acetic acid and dilute mineral acids; it dissolves in concentrated sulfuric acid with a yellow-green fluorescence. Golden yellow leaflets (from toluene).

Found %: N 3.31, 3.19. $C_{19}H_9NCl_2Br_2$. Calculated %: N 2.91.

SUMMARY

1. A number of new polyhalo derivatives of 2-aminotriphenylcarbinol were synthesized by reacting mono- and dihalo derivatives of methyl anthranilate with p-chlorophenylmagnesium bromide, and their properties were studied.

2. Based on halo derivatives of 2-aminotriphenylcarbinol, a method was developed for preparing di- and polyhalo derivatives of 9-phenylacridine with the halogens located in different benzene rings; here we obtained a number of previously unknown compounds and studied their properties.

Received April 8, 1957

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STUDY OF THE STEPHEN REACTION*

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In 1925 Stephen described [2] a method of obtaining aldehydes by the reduction of nitriles with stannous chloride in anhydrous ether, saturated with hydrogen chloride, followed by hydrolysis of the intermediate aldimine salt.**

$$RCN \xrightarrow{SnCl_2;\ HCl} [RCH{=}NH]_2 \cdot H_2SnCl_6 \xrightarrow{H_2O} RCHO$$

This method usually gives good results when preparing aldehydes of the aromatic series, but the yields of aliphatic aldehydes fluctuate greatly and for the most part are quite low [7, 10, 12-16] (the data of Stephen on nearly quantitative yields of such aldehydes as phenylacetaldehyde and cinnamaldehyde could not be duplicated [14, 17]). When other investigators attempted to adapt the Stephen method it was found that the time, indicated by Stephen himself, is slightly too short to achieve complete reaction (see, for example, [14]), and that the procedure originally recommended by him to purify anhydrous stannous chloride cannot be duplicated [18]. The vagueness of Stephen's statements led to the situation that the conditions, chosen by later investigators, were often fortuitous to variable degree; thus, in not a single case was the optimum reaction temperature*** established, or the influence of water, present in the reaction mixture****, on the yield of aldehyde. Finally, it should be mentioned that the aldimine salt with chlorostannic acid, formed in the reaction, does not always deposit in the precipitate. However, following Stephen's recommendations, in most cases only the precipitate of this salt was hydrolyzed to obtain the aldehyde, without investigating the mother liquor (compare [21]).

In the course of our studies on the synthesis of amino acids labeled with radioactive carbon the need arose to use the Stephen reaction for the preparation of some aliphatic aldehydes from the corresponding nitriles. Since in this case the Stephen method up to now has given only poor results, we were forced to determine on the example of obtaining one of the aliphatic aldehydes (isovaleraldehyde) the optimum conditions for its formation. These conditions were then extended to the synthesis of other aldehydes, namely acetaldehyde and phenylacetaldehyde.

The following was determined as a result of our studies. 1) The aldimine salt with chlorostannic acid, a direct product of reaction, can show variable solubility in the reaction medium. Thus, the phenylacetaldimine salt deposits completely in the precipitate, whereas the acetaldimine salt remains partially in solution, while the isovaleraldimine salt is completely soluble.* For this reason in studying each new case of the Stephen reaction it is necessary to investigate not only the precipitate, separating from the reaction mixture, but also the residue, remaining after evaporation of the solvent.

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* Communication VII of the series "Investigations of compounds labeled with C^{14} and N^{15}." For previous communications see [1].

** For reviews on the Stephen reactions see [3, 4]; for papers not cited in these reviews see [5-11].

*** For example, Knight and Zook [19] ran the process at 0°, while King and co-workers ran it at the boiling point of ether [12, 13, 20].

**** Slotta and Kethur [18] added water to the reaction mixture, although Stephen recommended running the process in anhydrous ether medium.

2) The optimum reaction temperature lies in the limits 15-25°. This data, obtained on the example of reducing isovaleronitrile (see Table 1), also proved valid for both acetonitrile and phenylacetonitrile. Raising the reduction temperature leads to a sharp drop in the yield of aldehyde. The reason for this is cleavage of the diethyl ether by the hydrogen chloride, leading to the formation of alcohol, which converts unreacted nitrile to the imino ester. The formation of the latter was shown in the case of isovaleronitrile by the isolation (after hydrolysis of the reaction mixture) of ethyl isovalerate. If the reduction was run at 100°, then the yield of this ester reached 25%. Small amounts of esters were also shown to be present when isovaleronitrile and phenylacetonitrile were reduced at room temperature (in these cases the esters were converted to the amides for identification). Consequently, concurrently with the reduction of nitriles there is a second process – conversion of the nitriles to imino esters, which can completely suppress the reduction reaction when the temperature is raised.

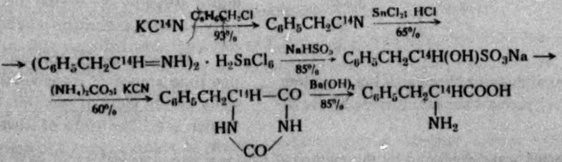
3) The optimum time for the reduction reaction is 7 days. Running the reaction for a longer time does not lead to any material increase in yield, while a shorter reaction time leads to a decrease in yield, which was shown on the example of preparing isovaleraldehyde (see Table 2) and confirmed on the example of phenylacetaldehyde.

4) The optimum amount of stannous chloride in the preparation of isovaleraldehyde is 7 moles per mole of nitrile, while further increase in the $SnCl_2$ is practically without value (see Table 3). However, in the reduction of phenylacetonitrile it proved possible to reduce the amount of $SnCl_2$ to 2.5 moles per mole of nitrile without reducing the yield of aldehyde.

5) The presence of water in the reaction mixture causes the yield of aldehyde to drop, which was shown on the example of reducing isovaleronitrile (see Table 4).

In summary, it was established that under the optimum conditions the yield of isovaleraldehyde is 61-64%; the yield of acetaldehyde under the optimum conditions is 64-67%, and that of phenylacetaldehyde is 55-60% (as the bisulfite compound). Evidently, aliphatic and aralkyl aldehydes are formed in relatively smaller yields than most aromatic aldehydes (compare [3]) for the reason that in preparing the first two types the time required to reduce the nitriles is much longer than in the case of the last type (7 days instead of 5-24 hrs). During this time the hydrogen chloride succeeds in cleaving a substantial amount of diethyl ether with the formation of alcohol, and consequently a substantial amount of imino ester is formed as the result of unreacted nitrile reacting with the alcohol. This circumstance is responsible for a greater reduction in the yield of aliphatic aldehydes when compared to the aromatic aldehydes. For this reason it is in general impossible to use the Stephen method to reduce those nitriles that contain groupings capable of decomposing the intermediate chlorimines (compare, for example, the negative result obtained in the reduction of β-hydroxypropionitrile [14]). It would be desirable in the future to search for such solvents for the Stephen reaction as would be less prone to cleavage by hydrogen chloride than diethyl ether.

The reduction of phenylacetonitrile to phenylacetaldehyde by the Stephen method was used by us to synthesize phenylalanine-2-C^{14}, starting with $KC^{14}N$. The yield of labeled phenylalanine was 25-26%, based on $KC^{14}N$.



$$KC^{14}N \xrightarrow[93\%]{C_6H_5CH_2Cl} C_6H_5CH_2C^{14}N \xrightarrow[65\%]{SnCl_2;\ HCl}$$

$$\rightarrow (C_6H_5CH_2C^{14}H{=}NH)_2 \cdot H_2SnCl_6 \xrightarrow[85\%]{NaHSO_3} C_6H_5CH_2C^{14}H(OH)SO_3Na \rightarrow$$

$$\xrightarrow[60\%]{(NH_4)_2CO_3;\ KCN} \begin{array}{c} C_6H_5CH_2C^{14}H-CO \\ HN \quad\; NH \\ CO \end{array} \xrightarrow[85\%]{Ba(OH)_2} \begin{array}{c} C_6H_5CH_2C^{14}HCOOH \\ NH_2 \end{array}$$

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[*] It should be mentioned that the solubility of these salts in water is similar to their solubility in ether, saturated with HCl. Thus, the phenylacetaldimine salt, in contrast to the two other salts, is insoluble in both HCl-saturated ether and water. This circumstance makes hydrolysis of the given salt difficult, and to avoid polymerization of the aldehyde as it is formed it is expedient to convert the aldehyde directly to the bisulfite compound by boiling with bisulfite solution.

Many other amino acids, labeled with C^{14} in the α-position, can be synthesized by a similar procedure. An advantage of the proposed method of synthesizing 2-C^{14}-amino acids is the small number of steps involved, in which respect it differs favorably from all of the earlier described methods of introducing tracer elements in the α-position of amino acids.

EXPERIMENTAL

1. Determination of optimum conditions for preparation of isovaleraldehyde. Anhydrous stannous chloride* and absolute ether, the latter containing not more than 0.01-0.03% water (determined by the K. Fischer method), were placed in a flask. The amount of ether taken was 1 ml per millimole of $SnCl_2$. The flask was attached to a head which was fitted with tubes (with stopcocks) for the admission and escape of gas, and also a dropping funnel. Hydrogen chloride, thoroughly dried by passage through H_2SO_4 and $Mg(ClO_4)_2$, entered the flask through the inlet tube, while the outlet tube was connected to a Tishchenko flask, containing concentrated H_2SO_4. With water cooling, a stream of hydrogen chloride was passed into the mixture until all of the stannous chloride had dissolved and two liquid layers were obtained.** Then either 1.00 ml (9.55 mmoles) of isovaleronitrile or its solution in absolute ether was added through the funnel (using the air pressure of a rubber bulb), the funnel rinsed twice with 1-2 ml of absolute ether, and then hydrogen chloride was again passed into the solution until completely saturated. The reaction mixture was allowed to stand for a certain length of time at the desired temperature, then the ether and hydrogen chloride were removed on the water bath (at the end using a water-jet pump), 100 ml of water was added to the residue, and the mixture was subjected to distillation for 30 min. The aldehyde in the distillate was determined either by the oxime method [24] or gravimetrically as the 2,4-dinitrophenylhydrazone.

TABLE 1

Effect of Reaction Temperature on Yield of Isovaleraldehyde (2 moles of $SnCl_2$ per mole of nitrile)

Reaction time	Temperature	Yield (in %)
7 days	0°	15
7 "	15-25	32
7 "	37	15
3 hrs	100	0

TABLE 2

Effect of Reaction Time on Yield of Isovaleraldehyde (7 moles of $SnCl_2$ per mole of nitrile; temperature 15-25°)

Reaction time (in days)	Yield (in %)
1	31
3	40
5	49
7	61-64
14	65

TABLE 3

Effect of Amount of $SnCl_2$ on Yield of Isovaleraldehyde (Reaction time 7 days; temperature 15-25°)

Number of moles of $SnCl_2$ per mole of nitrile	Yield (in %)
2.0	32
4.0	46
7.0	61-64
9.4	66

TABLE 4

Effect of Amount of Water on Yield of Isovaleraldehyde* (7 moles of $SnCl_2$ per mole of nitrile; reaction time 7 days; temperature 15-25°)

Number of moles of water per mole of nitrile	Yield (in %)
0	61-64
3.6	32-47
7.0	25
14.0	< 5

* The water was added as either partial or complete replacement of anhydrous stannous chloride by the dihydrate.

The data on the influence of temperature, reaction time, amount of stannous chloride and addition of water on the yield of isovaleraldehyde are given in Tables 1-4. The yield of isovaleraldehyde under the optimum conditions (15-25°, reaction time 7 days, amount of $SnCl_2$ 7 moles per mole of nitrile) is 61-64%.

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* Stannous chloride was dehydrated by the method of [22] in a vacuum-desiccator over sulfuric acid for a week. The treatment recommended by Stephen [23] of using acetic anhydride to dehydrate stannous chloride dihydrate yields a reducing agent of inferior quality. The attempted recrystallization of anhydrous stannous chloride from pyridine [2] leads to decomposition of the reagent; see also [18].

** The absence of two layers means that water is present in the reaction mixture, which causes the yield of aldehyde to drop; such a solution cannot be used for the reduction.

2. Preparation of acetaldehyde. The reaction was run using the optimum conditions described in Expt. 1 for the preparation of isovaleraldehyde. A yellow precipitate was obtained as a reaction result, from which we isolated $^7/_8$ of the obtained aldehyde, while the other $^1/_8$ was in the solution. However, it is more expedient not to isolate the precipitate, but instead to treat it together with the solution in the manner described in Expt. 1. The yield of aldehyde was 64-67%.

3. Preparation of phenylacetaldehyde. a) Preparation of phenylacetaldimine salt with chlorostannic acid (for the conditions see Expt. 1). A mixture of 25 ml of absolute ether and 5 g of $SnCl_2$ (2.6 mmoles) was placed in the apparatus flask. The mixture was saturated with hydrogen chloride and then 1.1 ml of benzyl cyanide (9.6 mmoles) was added. After 7 days the precipitate was suction-filtered, washed with absolute ether, and dried in a vacuum-desiccator over either NaOH or H_2SO_4; weight 1.8-2.5 g.*

The salt, prepared for analysis, was suction-filtered in the absence of atmospheric moisture and then washed with absolute ether that had been saturated with hydrogen chloride. The salt was obtained as a white crystalline substance that slowly liberated the aldehyde when kept in the air.

Found %: Sn 20.55, 20.60; N 4.68, 4.73; Cl 37.68, 37.87. $[C_8H_9N]_2 \cdot H_2SnCl_6$. Calculated %: Sn 20.76; N 4.90; Cl 37.21.

b) Preparation of bisulfite compound of phenylacetaldehyde. The aldimine salt (1.3 g) was added to a solution of $NaHSO_3$, obtained by saturating a suspension of 5.8 g of $NaHCO_3$ in 20 ml of water and 2 ml of butanol with SO_2. The mixture was refluxed for 2 hrs (heating in an oil bath), the obtained precipitate was suction-filtered and washed with water, and the filtrate was evaporated to dryness. About 5.8 g of substance was obtained here, containing 13-16% of the phenylacetaldehyde bisulfite compound; the phenylacetaldehyde was determined as the 2,4-dinitrophenylhydrazone (see [26]). If analytically pure aldimine salt was used, the yield of phenylacetaldehyde was 85%. The yield of phenylacetaldehyde, based on the starting nitrile, was usually of the order of 55-60%.

4. Preparation of phenylalanine-2-C^{14}. Radioactive benzyl cyanide (2.1 ml), purified by distillation (for its preparation from benzyl chloride and $KC^{14}N$ see [25]), was reduced by the Stephen method under the conditions of Expt. 3a. The obtained 3.35 g of phenylacetaldimine salt with chlorostannic acid (yield 65%) was converted to the bisulfite compound as described in Expt. 3b. A mixture of 15.1 g of the isolated bisulfite compound (phenylacetaldehyde content 14.7%), 0.98 g of potassium cyanide, 6.5 g of ammonium carbonate, 24 ml of 25% aqueous ammonia and 12 ml of alcohol was heated with constant shaking in a sealed tube at 100° for 1 hr. The obtained 5-benzylhydantoin (weight 1.13 g, yield 60%) was isolated using the conditions described earlier in the synthesis of 1-C^{14}-tyrosine [26]. The hydantoin was heated with constant shaking for 1 hr at 150-160° in a sealed tube with 3 g of $Ba(OH)_2 \cdot 8H_2O$ and 16 ml of water. The precipitate of barium carbonate was suction-filtered, washed with hot water, the filtrate treated with 0.7 g of ammonium carbonate, the precipitate filtered, the filtrate evaporated to dryness, and the phenylalanine-2-C^{14} transferred to a suction-filter funnel using 5-8 ml of alcohol. Yield 0.85 g (86%); m. p. 256-257° (with decomp.).

SUMMARY

1. The conditions for the preparation of aliphatic and aralkyl aldehydes, and specifically of acetaldehyde, isovaleraldehyde and phenylacetaldehyde, by the Stephen reaction were investigated.

2. It was shown that together with reduction of the nitriles to aldimines there is a concurrent transformation of the nitriles to imino esters, proceeding due to reaction with the alcohol formed in the cleavage of diethyl ether with hydrogen chloride. By raising the temperature it is possible for the reduction of the nitrile to be completely suppressed by the latter process.

3. The reduction of benzyl cyanide to phenylacetaldehyde by the Stephen method was utilized to synthesize phenylalanine-2-C^{14}, starting with $KC^{14}N$.

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* If the reaction time is reduced to 1-3 days, then the amount of obtained salt remains approximately the same, but the yield at the stage of obtaining the bisulfite compound of the aldehyde shows a sharp drop.

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Received March 18, 1957

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* Original Russian pagination. See C. B. translation.

THE POLYMERIC PEROXIDE OF VINYL CHLORIDE

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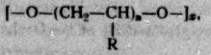
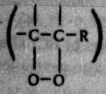
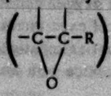
As has been noted several times in the literature, vinyl monomers react with oxygen to form peroxide compounds. Polymeric peroxides have been isolated in a series of cases for some vinyl compounds: diphenylethylene [1], α-terpilene [2], styrene [3, 4], indene [5], chloroprene [6], methyl methacrylate [7], vinyl acetate [7], 2,3-dimethylbutadiene [8], acrylonitrile [9], α-methylstyrene [10] and methacrylonitrile [11] and their structures may be expressed by the general formula



$$[-O-(CH_2-\underset{\displaystyle R}{\underset{|}{CH}})_n-O-]_x,$$

where $n \geq 1$, depending on the nature of the monomer and experimental conditions.

When monomers reacted with oxygen, two types of reactions were noted: the formation of polymeric peroxides and of carbonyl compounds. Hydroperoxide and carbonyl end groups were identified. In addition, cyclic  or epoxide  structures were proposed for the end groups [3].

In a series of cases, the decomposition products of polyperoxides of vinyl compounds were determined. In most cases the decomposition occurred in such a way that the break in the peroxide (−O−O−) bonds was accompanied by rupture of the adjacent (−C−C−) bonds to form a mixture of formaldehyde and the carbonyl compound corresponding to the given monomer; the polymeric peroxide of styrene decomposed to formaldehyde and benzaldehyde; methacrylonitrile polyperoxide − to formaldehyde and pyruvonitrile; methyl methacrylate polyperoxide − to formaldehyde and methyl pyruvate; diphenylethylene polyperoxide − to formaldehyde and diphenyl ketone, etc.

The peroxides of chlorovinyl compounds have hardly been studied. Reinhardt [12] described vinylidene chloride peroxide, whose structure was not established accurately. This peroxide was formed by the action of atmospheric oxygen on vinylidene chloride at −40° and +25° and could initiate the polymerization of this monomer. The peroxide itself was readily exploded by heating or by a slight mechanical blow. Slow decomposition of vinylidene chloride peroxide gave formaldehyde, phosgene and hydrogen chloride. The peroxide compounds of vinyl chloride were not investigated. It is only known that the existence of an induction period during the polymerization of this monomer is explained by the monomer reacting with oxygen [13]. We could not find any more detailed data on chlorovinyl peroxide compounds.

We showed [14] that in polymerizing vinyl chloride in the presence of air, at first only peroxide compounds were formed until the complete disappearance of oxygen from the gas phase.

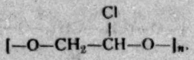
The aim of the present work was to isolate peroxide compounds of vinyl chloride and to establish their structures. In addition, as oxygen is almost always found in greater or smaller amounts in the polymerization of vinyl chloride in production reactors, it seemed interesting to study the properties and reactivity of the polymeric peroxide and to elucidate its effect on the quality and properties of the polymer produced.

During the induction period in the mass polymerization of vinyl chloride in the presence of molecular oxygen, a yellowish viscous liquid was obtained which vigorously liberated iodine from an acetic acid solution of potassium iodide. It decomposed with an explosion when brought near a naked flame and also when ground with a glass rod under water. In the latter case characteristic crackles from explosions could be heard.

Due to the instability of the compounds being investigated and the difficulty of obtaining sufficiently large amounts (all the operations were carried out with several tens of milligrams, prepared for each experiment separately) reprecipitated vinyl chloride peroxide could not be isolated. As a result of these circumstances, the quantitative determinations could be low in comparison with the calculated ones.

One could assume that on oxidizing vinyl chloride, the polymeric peroxide is formed by the copolymerization of vinyl chloride and oxygen. This hypothesis was confirmed by the determination of peroxide compounds formed at 50° during the induction period in 1 g of vinyl chloride, containing 0.5% by weight of azoisobutyrodinitrile as an indicator, as these results showed [14] that the amount of peroxide compounds of this monomer in the reaction mixture increased up to the moment when this monomer started precipitating at a constant rate, equivalent to 0.073 ml of $Na_2S_2O_3$/hr. The first order decomposition constant of the azoisobutyrodinitrile at this temperature was 0.0107 hr^{-1} [15]. It follows from this that if every radical formed participated in the chain growth reaction, then in an hour a peroxypolymer would be formed with an average degree of polymerization of $P = 6\text{-}7$. Actually, the value may be somewhat higher as some of the radicals are used up in side reactions [16].

The formula of the ideal 1 : 1 copolymer of oxygen and vinyl chloride should be



$$[-O-CH_2-\overset{\overset{\displaystyle Cl}{|}}{C}H-O-]_n.$$

As can be calculated readily, a sample of polyperoxide should contain 33.86% of oxygen and 37.59% chlorine. The ratio $\frac{\%O}{\%Cl} = 0.903$.

The average oxygen content determined iodometrically from a whole series of experiments was 26.7% (26.0-27.8%), which is less than that calculated. Determination of HCl after hydrolysis of the peroxide with water at 60-70° also gave a low chlorine content – 29.3%. The ratio $\frac{\%O}{\%Cl} = 0.911$.

As the polymeric peroxide of vinyl chloride was not purified or recrystallized, one may assume that considering the very close values of $\frac{\%O}{\%Cl}$, the given compounds had, in all probability, a 1 : 1 structure with regular sequences of the units $(-CH_2CHClOO-)$.

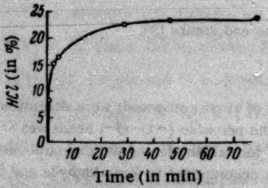


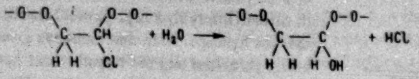
Fig. 1. HCl evolution kinetics during hydrolysis of the polyperoxide with water.

The infrared spectrum of the vinyl chloride peroxide in a carbon tetrachloride solution had an intense, wide absorption band at 883 cm^{-1}, which is characteristic of peroxide compounds and due to the $-O-O-$ bond, and a strong absorption band at 1080 cm^{-1}, which could have been due to the presence of the $-\overset{|}{\underset{|}{C}}-O-O-$ group [17]. The presence of hydroperoxide groups was not shown clearly. It was shown [17] that this group forms the following bands in an IR spectrum: 840 cm^{-1} (O–O–H), 880 cm^{-1} (O–O), 3450 cm^{-1} (O–H) and 6800 cm^{-1} (1st overtone of O–H bond).

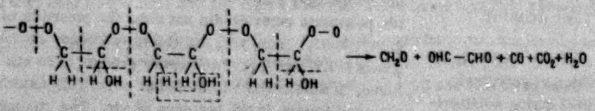
The peroxide being investigated had no bands at 3450 and 6800 cm^{-1} and the band at 817 cm^{-1}, which could probably be explained by $-O-O-H$ group vibrations, was extremely weak. There was also no absorption band in the region of 1170 cm^{-1}, which is assigned to the ether group $-\overset{|}{\underset{|}{C}}-O-\overset{|}{\underset{|}{C}}-$ [18].

The exceptional lability of the chlorine atom in the polyperoxide of vinyl chloride should be noted. Even during hydrolysis in the cold, the chlorine was eliminated from the polymeric molecule at a high rate (Fig. 1). This is not surprising as the capacity of α-chloro substituted ethers for hydrolysis by water is well known. It follows from this that molecular oxygen is not only an inhibitor of vinyl chloride polymerization, but also, due to the rapid hydrolysis of polymeric peroxides, formed during the polymerization induction period, it lowers the pH of the reaction medium. This has a negative effect on the optimal conditions for the decomposition of initiators, the yield and properties of the polymer and strongly affects conjugated solution [19], which is important not only for emulsion but also bead polymerization.

The polyperoxide of vinyl chloride reacted with water even in the cold to split out a chlorine ion quantitatively to form HCl; at a higher temperature (50°) it decomposed. Among the products were found HCl, formaldehyde, glyoxal, CO and CO_2. In accordance with this, the polymeric peroxide of vinyl chloride is decomposed by water in two stages:

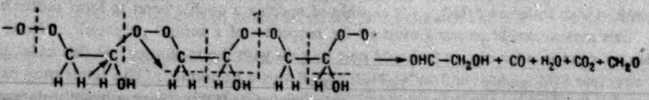


(1)



(2)

It should be noted that glyoxal $(CHO)_2$ was identified by the formation of the osazone by 2,4-dinitrophenylhydrazine. However, exactly the same osazone may be formed by glycoaldehyde, which could also be a possible decomposition product of vinyl chloride polymeric peroxide



(3)

Decomposition by this equation gives carbon monoxide, hydrogen chloride and glycolaldehyde. Carbon monoxide in this case may be formed by the peroxide oxygen atom attacking a formaldehyde molecule, apparently at the moment of decomposition.

Data in the work of Strause and Dyer [11] on the oxidation of methacrylonitrile, supports such a hypothesis. They considered that carbon monoxide and dioxide, produced in the decomposition of polymeric methacrylonitrile peroxide, were formed as a result of formaldehyde oxidation and this was intensified by ultraviolet radiation.

A balance of the decomposition products may be used to decide between the two possible decomposition schemes, (2) and (3) (see Table 1). If we consider decomposition by Eq. (2) only, we do not find a considerable amount of the products (~ 15%); however, calculating by Eq. (3), we find, on the contrary, an excess of them (~ 10%). Taking into account the possible inaccuracies in the determination, it is difficult to decide on the possibility of decomposition by one or other scheme due to the small amounts of material analyzed.

As CO_2 was formed from the end groups, independent of decomposition schemes (2) or (3), if one tentatively assumes that the number of CO_2 molecules corresponds to the number of polymeric peroxide molecules and that the number of HCl molecules corresponds to the number of $(-CH_2CHClOO-)$ units in the chain, then in various experiments the ratio $\frac{HCl}{CO_2} = 17\text{-}26$, which gives an average molecular weight of 1600-2500.

Experiments on the initiation of the polymerization of various monomers by vinyl chloride polymeric peroxide showed that it induced polymerization of styrene, vinylidene chloride, vinyl chlorine, butyl methacrylate and methacrylic acid.

It was noted in many works in which the polymerization capacity of polyperoxides was studied, that the process was due to radicals, formed during the decomposition of polymeric peroxides [11, 20]. This conclusion does not always agree with experimental material as such a decomposition would have led to a sharp increase in the rate of polymerization and to an ever increasing capacity of the monomer for absorbing oxygen from the gas phase. Actually, the amount of peroxide compounds grows linearly with time [14]. Some data show that after the induction period in vinyl chloride polymerization, there is a slight increase in the rate of the true polymerization.

Miller and Mayo [3] found that the increase in the rate of formation of polymeric styrene peroxide in the presence of 0.01 M of polyperoxide was by a factor of only 1.7, while an equal amount of azoisobutyrodinitrile increased the rate of polyperoxide formation by a factor of 55.

In all probability polymeric peroxides are not only capable of splitting by a free radical mechanism and then initiating true polymerization, but also act as stable radicals $R(MO_2)_x\cdot$ with an extended life time. The existence of such a radical was confirmed by the capacity of a polymeric peroxide solution in a monomer to decolorize a solution of diphenylpicrylhydrazyl in dichloroethane [21]. It follows from this that the hydroperoxide and carbonyl groups identified in certain polymeric peroxides and the hypothetical epoxy and cyclic end groups may not be the only possible ones. Actually, the IR spectrum of vinyl chloride polymeric peroxide did not show the presence of the $-O-O-H$ group clearly. However, the absorption bands characteristic of carbonyl groups (1725 cm^{-1}) [17] and epoxy groups (1170 cm^{-1}) [18] were not found. It should also be noted that paper [22] examined the polymerization of styrene in the presence of air. The changes in magnetic susceptibility showed that the radicals were stabilized by the action of oxygen and that their concentration in the reaction mixture increased. This observation agrees with our hypotheses.

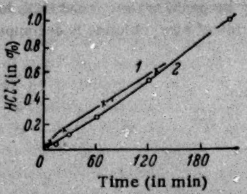


Fig. 2. Kinetics of HCl evolution in the thermal decomposition of polyvinyl chloride. 1) Obtained during polymerization initiated by polymeric peroxide (decomp. at 72°), 2) industrial (decomp. at 161.5°).

The radical with structure $R(MO_2)_x\cdot$ is capable of opening a double bond to form radicals of the type $R(MO_2)_xM_y$. This radical should possess almost all the properties of a normal polymeric radical of the type $RM\cdot_z$ and in the absence of molecular oxygen it should start to grow with the monomer. In this case, naturally, a polymer with the structure $R(MO_2)_xMy\cdot$ or $R(MO_2)_xMy(MO_2)_kR$ should be formed. The latter may be formed by the recombination of radicals of type $R(MO_2)_xM_y\cdot$ with polyperoxide radicals. Such a hypothesis was confirmed by investigating a polymer, obtained during the polymerization of vinyl chloride, initiated by its own polymeric peroxide. The preparation was first carefully washed with liquid vinyl chloride till it was completely freed from free peroxide and then washed three times with methanol. The polymer analyzed had a low chlorine content (54.44%), a low molecular weight (some samples had a molecular weight of 20,000-30,000) and an exceptionally low decomposition point ($<$ 70-80°), which for a normal polyvinyl chloride resin is of the order of 150°. Such a low decomposition point may be explained by the early breakdown of the polyperoxide ring of a polymeric molecule of the type $R(MO_2)_xM_y$. We plotted the kinetics of resin decomposition at 175° by the evolution of HCl, using an electroconductivity method. Figure 2 illustrates a typical experiment. It also shows the relation of HCl evolution to time for a resin obtained industrially and this appears as a straight or almost straight line with a certain tendency towards an increase in the elimination of HCl during the experiment. The line for the resin investigated shows a definite change of slope. HCl was evolved more rapidly in the first few minutes of the experiment which, apparently, was due to decomposition of the peroxide part $R(MO_2)_x$ of the polymer molecule. Then, after the change in slope, the rate of hydrogen chloride evolution, which apparently characterized the decomposition of the true polymer, M_y, continued at a much slower rate. The products of polymer decomposition by water at a high temperature were analyzed and the peroxide oxygen content determined in 1 g sample of the resin, in which was found HCl 0.0000347 mole, O_2 – 0.0000365 mole and $>CO$ 0.0000713 mole.

The amount of hydrogen chloride (0.13%) found in the polymer by this method practically coincided with the amount of HCl evolved by the polymer up to the moment when the rate of the thermal decomposition of the resin changed (Fig. 2, curve 1).

We concluded from the data obtained from investigating the properties of polyvinyl chloride, prepared by initiation of vinyl chloride with polymeric peroxide, that an unusual block polymer was produced, one part of which had a polyperoxide structure and the other the structure of a true polymer.

Thus, in vinyl chloride polymerization, molecular oxygen, besides having a strong inhibiting effect, also negatively affects the quality of the polymer obtained, by greatly lowering the decomposition point, the molecular weight and some other properties of the resin.

EXPERIMENTAL

The polymeric peroxides were prepared in sealed ampules of 70-80 ml capacity from 3-5 g of vinyl chloride and air in the gas phase at 45-50° with continuous agitation in a vibrating thermostat. After 8-10 hrs the ampules were removed and those which did not contain traces of polymer were opened. Their contents were transferred to a tared flask, filled with nitrogen and placed in a bath of snow, and the monomer distilled off. The flask was reweighed to determine the weight of the peroxide.

In some experiments, a very small amount of azoisobutyrodinitrile was added for determining the rate of polymeric peroxide formation.

The peroxide oxygen was determined by the usual iodometric method. Into the flask, containing the sample of peroxide, was introduced 3.5 ml of glacial acetic acid (chemically pure) and 11 ml of 5% potassium iodide in methanol. The methanol was first treated with active charcoal and then distilled twice.

The mixture was kept in the dark and the iodine liberated was titrated with 0.1 N hyposulfite solution.

Hydrolysis of vinyl chloride polymeric peroxide. The flask, containing the sample of peroxide examined (0.3-0.5 g), was placed on a water bath maintained at 50-60°. The gases liberated were passed through a small reflux condenser and collected in a Hempel burette and analyzed. The CO and CO_2 were found.

HCl and a mixture of aldehydes were identified in the aqueous phase. The aldehydes were isolated as the 2,4-dinitrophenylhydrazones, which were separated by paper chromatography [23] on acetylated paper [24].

A series of experiments established that we had at least two compounds to deal with. Identification of the components from the relative movements of the concentration maxima of the substances, $R_f = a/b$ (where a is the movement of the concentration maximum of the substance in centimeters and b is the movement of the solvent

TABLE 1

Composition of Decomposition Products of Polymeric Peroxide of Vinyl Chloride

Sample of polyperoxide (g)		0.3470	0.4200	0.4002
Found	CO	32.4ml 0.0406 g	39.6 ml 0.0495 g	38.1 ml 0.0477 g
	CO_2	2.8 ml 0.0052 g	5.2 ml 0.0102 g	2.9 ml 0.0057 g
	$\overset{\text{O}}{\overset{\|}{-\text{C}-}}$groups (g)	0.0555	0.0980	0.0835
	HCl (g)	0.089	0.1463	0.1210
Amount of polyperoxide, relative to HCl, considering a 1:1 structure (g)		0.230	0.378	0.313
Molecular weight of polymeric peroxide (from CO_2)		1740	1640	2420
Amount of formaldehyde (in g), contained in decomposition products of the polyperoxide, calc. by scheme (2)		0.0435	0.0530	0.0511
Amount of glyoxal (in g), contained in the polyperoxide decomposition products, calc. by scheme (2)		0.0209	0.0458	0.0370
Balance of polyperoxide decomposition products, calc. by scheme (2)		0.1991	0.3048	0.2625
Amount of glycoaldehyde (in g), contained in polyperoxide decomposition products, calc. by scheme (3)		0.1300	0.2100	0.1790
Balance of polymeric peroxide decomposition products (in g), calc. by scheme (3).		0.2647	0.4160	0.3534

front), showed the presence of formaldehyde hydrazone and the osazone of an unknown compound in the mixture. The osazone spot gave a blue color when treated with alcoholic alkali in contrast to the hydrazone, which gave a blood red color. For formaldehyde we found R_f 0.37-0.39, while according to [21] the R_f is 0.38. The R_f of a reference spot was within these limits.

Using the different solubilities in alcohol, we washed out the osazone from the hydrazone by washing the mixture several times with alcohol.

From analysis data and melting point, the compound corresponded to the osazone of glyoxal. The m. p. was 306-309° and according to [25] it should be 311°.

Found %: C 39.20; N 25.80; H 2.49. $C_{14}H_{10}O_8N_8$. Calculated %: C 40.19; N 26.70; H 2.41.

The formation of formaldehyde was also confirmed by formation of the dimedone derivative [26] with m. p. 185°; a mixed sample melted at 185-185.5°.

Data from three experiments in which the decomposition products of the polymeric peroxide were determined quantitatively are given in Table 1.

The preparation of polymer using vinyl chloride polymeric peroxide was carried out by heating solutions of vinyl chloride polyperoxide in the appropriate monomer at 50° in sealed ampules in an atmosphere of nitrogen. Blank experiments were run in parallel. The ampules were filled with monomer and opened on a special apparatus [27].

In all cases, polymers were obtained. Vinyl chloride polymeric peroxide in concentrations of about 0.1 M produced polymerization of styrene after 20 hrs, of vinylidene chloride after 4 hrs, of butyl methacrylate after 20 hrs and of methacrylic acid after 15 hrs.

TABLE 2

Wavelength (μ)	Frequency (cm^{-1})	Intensity value	Group
12.35	817	Very weak	O—O—H
11.35	883	Broad	O—O
9.25	1080	Strong	C—O—O
7.55	1323	Average	CH (deformation)
7.53	1330	Average	
7.50	1333	Average	
6.20	1618	Weak	C—C
3.55	2810	Average	CH (bond)
3.40	2920	Average	

Decomposition of polymer with water. To a sample of the resin, weighing 1 g, was added 50 ml of water, after which the mixture was heated for 1 hr on a water bath at 80-90°. The aqueous phase was analyzed for HCl and CO groups. The HCl was determined by titration with 0.01 N alkali and the carbonyl groups by reaction with hydroxylamine hydrochloride.

Determination of the HCl evolution kinetics during thermal decomposition of the polymer obtained during the polymerization of vinyl chloride, initiated by the polymeric peroxide, was carried out by measuring the electroconductivity using the method described in [28]. 0.4 g of polyvinyl chloride was introduced into a vessel, which was placed in a thermostat at 175° ± 0.01. Then purified air and dried air was passed through the system at a constant rate of 0.3 liters/min. The hydrogen chloride, flushed out by the air, passed into a thermostated vessel, containing a known amount of distilled water, where the HCl was absorbed completely. After given time intervals, the electroconductivity of the HCl solution was measured.

Determination of the HCl evolution kinetics, during the decomposition of the polymeric peroxide with water (Fig. 1), was carried out by measuring the electroconductivity by a procedure similar to that described above.

The difference was that the sample of peroxide was introduced directly into the thermostated vessel, which was then charged with a determined amount of distilled water with a known electroconductivity.

Data of spectroscopic investigation.* The infrared spectrum of a solution of the polymeric peroxide in carbon tetrachloride is given in Table 2.

SUMMARY

1. The polymeric peroxide of vinyl chloride was isolated. Its properties and hydrolysis and initiation capacities were investigated.

2. The polymer obtained by initiating the polymerization of vinyl chloride with the polymeric peroxide, had a low decomposition point and a lower molecular weight than the polymer prepared with the normal initiators. A structure was proposed for this polymer.

3. A decrease in the pH of the reaction medium in suspension polymerization of vinyl chloride may be caused by the presence of molecular oxygen from the hydrolysis of polymeric peroxides, formed during the induction period.

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* The IR-spectroscopic analysis of the polymeric peroxide was carried out by A. I. Finkel'shtein and the authors would like to thank him for it.

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Received December 15, 1957

REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

IV. REACTION OF BENZENE WITH POLYHYDRIC ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

I. P. Losev and O. V. Smirnova

In previous investigations on the reaction of benzene with alcohols in the presence of acid catalysts, we confirmed the hypothesis that primary alcohols are difficult to condense with benzene; this reaction proceeds much more readily with secondary and tertiary alcohols.

A study of the reaction of benzene with various polyhydric alcohols in the presence of acid catalysts is interesting as a possible means of preparing new saturated and unsaturated benzene derivatives (phenylpropanols, phenylbutylene, etc.) suitable for the synthesis of plasticizers and polymeric compounds.

We based our procedure for reacting benzene with diols on data from the investigations of various authors, published in the literature [1-8]. We first condensed benzene with butanediol-1,4 in the presence of H_3PO_4 and $AlCl_3$. However, under these conditions, no individual products could be isolated besides tarlike reaction products which were readily soluble in the normal organic solvents. Therefore, further investigations were carried out with butanediol-1,3. In this case the formation of two substances was possible: the reaction product of benzene 1) with the secondary alcohol group, 3-phenylbutanol-1 (I) and 2) with both alcohol groups, 1,3-diphenylbutane (II). In fact, both these substances were obtained and characterized, with 3-phenylbutanol-1 as the main product (up to 45.4% yield).

The dehydration of (I) was a separate problem, as it is known from the literature [9, 10] that lengthening the radical of a particular alcohol makes its dehydration more difficult. The dehydration was carried out under the conditions recommended for the dehydration of primary phenylethyl alcohol [9, 11, 12]. As catalysts we used H_2SO_4, NaOH, grade "M" cation-exchange, tar adsorbent, silica gel, alumina gel and aluminosilica gel. The best yield of 2-phenylbutene-3 (III) (56%) was obtained in the presence of aluminosilica gel at 140-160°. Under these conditions the catalyst may be regenerated completely.

On the basis of literature data [13-16] one could assume that the olefin we prepared would polymerize much more slowly than styrene and α-methylstyrene. Actually, none of the attempts to polymerize (III) in a pure form in the presence of benzoyl peroxide, $AlCl_3$ and BF_3 gave positive results. Therefore, we then used copolymerization of (III) with styrene. For this we tested various component ratios. Polymerization was carried out by heating to 60-70°. The addition of 1, 5 and 10% of (III) to styrene very slightly retarded the polymerization of the latter.

We then investigated the condensation of benzene with glycerol in the presence of H_3PO_4, $AlCl_3$, $FeCl_3$, H_2SO_4. Positive results were obtained in the presence of $AlCl_3$, at 100-102° and 5.5-6.0 atmos in an autoclave. The reaction gave two products: 2-phenylpropanediol-1,3 (IV) and 2,3-diphenylpropanol-1 (V).

EXPERIMENTAL

a) Condensation of benzene with butanediol-1,3 in the presence of $AlCl_3$. The reaction mixture consisted of 234.0 g (3 moles) of benzene, 90.0 g (1 mole) of butanediol-1,3 and 266.0 g (2 moles) of $AlCl_3$. The mixture was heated in a flask with a reflux condenser at 92-93°. The reaction was continued until the evolution of HCl ceased. The mixture was then poured into cold water and the product separated from the aqueous acid layer, washed until neutral, dried and distilled at 1-3 mm. From the distillation we obtained 4 fractions.

The 1st fraction was a mixture of the starting butanediol-1,3 and reaction products.

The 2nd fraction was redistilled to give a product with b. p. 120-122° at 22 mm (236-238° at atmospheric pressure), which corresponded to 3-phenylbutanol-1 (I). The yield was 45.4%.

d^{20}_4 0.9821, $n^{20}D$ 1.5160, MR_D 49.7; calculated 49.3. Found %: C 80.35, 80.40; H 9.6, 9.76; OH 11.21. M 148.4. $C_{10}H_{14}O$. Calculated %: C 80.00; H 9.33; OH 11.3. M 150.0.

To establish the structure of (I), it was oxidized in acetic acid with potassium bichromate. For the reaction we used 4.0 g of (I), 65 ml of acetic acid, 8.6 g of potassium bichromate and 8.5 ml of water. The reaction was performed at 80-90°. From the oxidation we obtained a product with b. p. 115° at 2 mm (223-225° at atmospheric pressure) in 25% yield and this was 3-phenylbutyraldehyde.

Found %: C 81.24, 81.47; H 8.51, 8.62. M 148.8. $C_{10}H_{12}O$. Calculated %: C 81.08; H 8.10. M 148.0.

The presence of an aldehyde group was confirmed by qualitative reactions.

On standing in air, the 3-phenylbutyraldehyde was converted into a white crystalline substance with m. p. 37-38°, which corresponded to 3-phenylbutyric acid.

The 3rd fraction was redistilled to give a product with b. p. 196-198° at 2 mm (298-300° at atmospheric pressure).

d^{20}_4 0.991, $n^{20}D$ 1.5217. Found %: C 91.84, 91.28; H 8.61, 8.48. M 208.5. $C_{16}H_{18}$. Calculated %: C 91.43. H 8.57; M 210.0.

These data correspond to 1,3-diphenylbutane (II). To establish the structure of (II), it was oxidized with potassium bichromate in acetic acid at 80-90°. We used 2.6 g of 1,3-diphenylbutane, 8.6 g of potassium bichromate, 8.5 ml of water and 55 ml of acetic acid. Distillation of the oxidation products yielded a substance with b. p. 202°, which gave a positive reaction for acetophenone, and a substance with b. p. 268-270° and m. p. 76° (from benzene). The latter did not depress the melting point of phenylacetic acid.

The 4th fraction was a dark red, tarry mass, which solidified in air.

b) Dehydration of 3-phenylbutanol-1 in the presence of aluminosilica gel. We used 10.0 g of 3-phenylbutanol-1 and 20.0 g of sodium hydroxide. The reaction was performed in a copper flask. Water and the dehydration product began to distill off at 140°. After separation of the aqueous layer, the dehydration product was dried with baked copper sulfate, vacuum distilled, then dried with metallic sodium and redistilled in vacuum. We obtained a substance with b. p. 53-55° at 2 mm.

d^{20}_4 0.8805, $n^{20}D$ 1.5042, MR_D 44.41; calculated 44.31. Found %: C 89.59, 89.91; H 10.11, 9.89. Bromine number 119.0. M 129.8. $C_{10}H_{12}$. Calculated %: C 90.90; H 9.09. M 132.0.

The data corresponds to 2-phenylbutene-3 (III), which is not described in the literature and was characterized by us for the first time.

Polymerization of (III) in the pure form did not lead to positive results. Copolymerization of (III) with styrene in the presence of benzoyl peroxide (0.5%) at 70° for 15 hrs gave copolymers with 1.5 and 10% 2-phenylbutene-3 contents.

c) Reaction of benzene with glycerol in the presence of $AlCl_3$. The reaction mixture consisted of 62.0 g of glycerol, 156.0 g of benzene and 66.7 g of $AlCl_3$. The reaction was performed by heating the mixture up to 60° over 15 hrs. Two substances were isolated from the mixture of reaction products by distillation.

1) 2-Phenylpropanediol-1,3 (IV) appeared as an orange-red liquid with b. p. 130-132° at 5 mm.

d^{20}_4 1.1161, $n^{20}D$ 1.5863, MR_D 43.4; calculated 43.16. Found %: C 71.12, 71.31; H 7.89, 7.98; OH 23.11. M 153.4. $C_9H_{10}(OH)_2$. Calculated %: C 71.06; H 7.93; OH 22.37. M 152.0.

2) 2,3-Diphenylpropanol-1 (V) appeared as a red liquid with b. p. 163-166° at 5 mm.

d^{20}_4 1.2147; $n^{20}D$ 1.6151, MR_D 65.2; calculated 65.8. Found %: C 84.02, 84.18; H 7.72, 7.78; OH 7.8. M 214.1. $C_{15}H_{15}(OH)$. Calculated %: C 84.90; H 7.55; OH 8.02. M 212.0.

The products obtained were readily soluble in alcohol, ether, benzene and acetone.

SUMMARY

1. The reactions of benzene with butanediol-1,4 and -1,3 were studied in the presence of phosphoric acid and aluminum chloride.

It was established that benzene reacted with butanediol-1,4 to form tarry products, and with butanediol-1,3 to give 3-phenylbutanol-1 and 1,3-diphenylbutane.

2. Dehydration of 3-phenylbutanol-1 in the presence of aluminosilica gel gave 2-phenylbutene-3.

3. Copolymerization of 2-phenylbutene-3 with styrene gave copolymers with various ratios of the starting components.

4. The reaction of benzene with glycerol in the presence of $AlCl_3$ was studied. This reaction gave 2-phenylpropanediol-1,3 and 2,3-diphenylpropanol-1, which were characterized.

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Received December 11, 1956

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*Original Russian pagination. See C.B. Translation.

REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

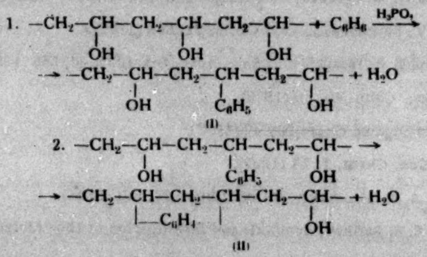
V. REACTION OF BENZENE WITH POLYVINYL ALCOHOL IN THE PRESENCE OF ACID CATALYSTS

I. P. Losev and O. V. Smirnova

In condensing benzene with cellulose [1], it was established that cellulose, dissolved in concentrated sulfuric acid, reacts with benzene and its homologs in the cold with considerable heat evolution; under these conditions three cellulose hydroxyl groups were substituted by aromatic radicals. There is no other data in the literature on the condensation of polyhydric alcohols with benzene.

We condensed benzene with polyvinyl alcohol using H_3PO_4 and $AlCl_3$ as catalysts. As a result a red-orange product was obtained, which swelled in water, alcohol, benzene and acetone. Oxidation of the reaction product with potassium bichromate gave phthalic anhydride and benzoic acid, which indicated the inclusion of phenyl rings in the polyvinyl alcohol chain.

The analysis data indicated that the reaction proceeded by the following scheme

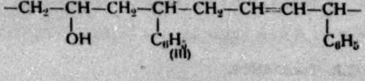


$$1.\ -CH_2-\underset{OH}{CH}-CH_2-\underset{OH}{CH}-CH_2-\underset{OH}{CH}- + C_6H_6 \xrightarrow{H_3PO_4} -CH_2-\underset{OH}{CH}-CH_2-\underset{C_6H_5}{CH}-CH_2-\underset{OH}{CH}- + H_2O \quad (I)$$

$$2.\ -CH_2-\underset{OH}{CH}-CH_2-\underset{C_6H_5}{CH}-CH_2-\underset{OH}{CH}- \rightarrow -CH_2-\underbrace{CH-CH_2-CH}_{C_6H_4}-CH_2-\underset{OH}{CH}- + H_2O \quad (II)$$

The number of hydroxyl groups, substituted by a phenyl ring, depended on the amount of catalyst and duration of the reaction. With all other reaction conditions equal, from 10 to 18% of the hydroxyl groups were substituted by phenyl radicals when the reaction time was varied from 7 to 14 hrs.

The products of reacting polyvinyl alcohol with benzene in the presence of $AlCl_3$ were examined by infrared spectroscopy using a 0.01 mm layer of the substance investigated [2, 3]. The analysis data established that the hydroxyl groups in the polyvinyl alcohol chain are partially substituted by phenyl radicals and as a result the polymer may acquire structure (I) and (II). The formation of double bonds is also possible at the same time and as a result the polymer may acquire structure (III).



$$-CH_2-\underset{OH}{CH}-CH_2-\underset{C_6H_5}{CH}-CH_2-CH=CH-\underset{C_6H_5}{CH}-$$

(III)

The presence of a double bond (III) could result in the formation of cross-links between the separate polymer molecules and this was confirmed by a decrease in the product's solubility after the reaction.

EXPERIMENTAL

1. Reaction of benzene with polyvinyl alcohol in the presence of H_3PO_4. The reaction mixture consisted of 22.0 g (0.5 mole) of polyvinyl alcohol, 117.0 g (1.5 mole) of benzene and from 12.7 g (0.1 mole) to 95.0 g (0.75 mole) of phosphoric acid (d 1.6, 77%).

The reaction was performed in a three-necked flask, fitted with a funnel, a Dean and Stark trap, a reflux condenser, a mercury seal and a paddle stirrer, which was heated to 80-82°. At the end of the reaction, the product was washed with hot water and dried at 50-60°. The results of the experiments are given in Table 1.

TABLE 1

Expt. no.	Amount of H_3PO_4 (in moles)	Duration of reaction (in hrs)	Hydroxyl group content* (in %)	Product yield (in %)	Remarks
1	0.10	7	30.1	5.8	Swelled in water, alcohols, and benzene
2	0.25	10	29.0	17.4	
3	0.25	14	27.3	28.0	
4	0.50	16	26.3	40.0	
5	0.75	10	33.5	—	Dissolved in water

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* With a 34% hydroxyl group content of the original polyvinyl alcohol.

To establish the structure of the reaction product, the latter was oxidized with potassium bichromate in an acetic acid medium. 7.0 g of the product was introduced into a three-necked flask, fitted with a stirrer and a reflux condenser, and the oxidizing mixture was added (16.0 g of $K_2Cr_2O_7$, 30 ml of CH_3COOH and 18 ml of H_2O). The oxidation was performed at 60-70° until complete solution occurred (5-6 hrs). After the reaction, the liquid reaction products, boiling in the range 43-59° at 5 mm, were distilled off from the reaction mixture. By sublimation the solid residue yielded a white substance, which formed needle-like crystals with m. p. 131-132° and b. p. 284-286°; they did not depress the melting point of phthalic anhydride.

The analysis data corresponded to phthalic anhydride and after removal of the phthalic anhydride, the reaction product was extracted with benzene in the hot. The benzene extract yielded crystals of benzoic acid (analysis and mixed melting point).

2. Reaction of benzene with polyvinyl alcohol in the presence of $AlCl_3$. The reaction mixture consisted of 22.0 g (0.5 mole) of polyvinyl alcohol, 117.0 g (1.5 mole) of benzene and from 33.3 g (0.25 mole) to 133.3 g (1.0 mole) of $AlCl_3$.

TABLE 2

Expt. no.	Amount of $AlCl_3$ (in moles)	Product yield (in %)	Remarks
1	0.25	6.7	Soluble in organic solvents
2	0.50	14.4	
3	0.75	23.6	
4	0.75	25.3	
5	1.00	26.7	

TABLE 3

Expt. no.	Duration of reaction (in hrs)	Product yield (in %)
1	6	18.0
2	12	28.6
3	18	29.0
4	24	50.6
5	26	51.0

The reaction was carried out under conditions similar to those of the previous experiments at 80-90° for 24 hrs. From the reaction we obtained two products, a liquid and a solid, which were then studied separately. The results of the experiments are given in Table 2.

The dependence of the product yield on the duration of the reaction is shown in Table 3 (benzene 1.5 mole, polyvinyl alcohol 0.5 mole and $AlCl_3$ 0.75 mole).

Liquid reaction product. Distillation yielded a fraction with b. p. 80-82° at 2 mm, corresponding to 1,3-diphenylpentane.

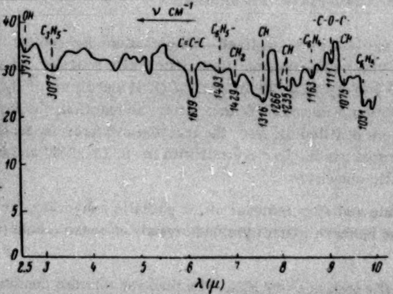
d^{20}_4 1.0318, $n^{20}D$ 1.6008, MR_D 73.2; calculated 73.8. Found %: C 90.86, 91.05; H 8.53, 8.73. M 226. $C_{17}H_{20}$. Calculated %: C 91.07; H 8.93. M 224.

Solid reaction product. After the separation of the benzene layer and the extraction of the acid and water-soluble products, the substance was separated into three fractions by successive precipitations with methyl alcohol. The results of the investigations are given in Table 4.

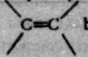
TABLE 4

Fraction no.	Hydroxyl group content (in %)	Specific viscosity	Yield (in %)	Remarks
1	32.0	0.2571	13.70	Soluble in water
2	31.0	0.2790	5.20	Soluble in water on heating
3	29.0	0.3834	3.75	Soluble in water on prolonged heating
Original polyvinyl alcohol	34.0	0.2125		

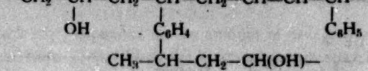
The 3rd fraction was examined further by infrared spectroscopy. The data are given in the figure.



Infrared absorption spectrum of the product from the reaction of polyvinyl alcohol with benzene in the presence of $AlCl_3$.

Bands found: at 3.25 μ (3077 cm^{-1}), 6.7 μ (1493 cm^{-1}), 8.6 μ (1163 cm^{-1}), 9.7 μ (1031 cm^{-1}), corresponding to the phenyl ring; at 2.65 μ (3751 cm^{-1}) – a hydroxyl group; at 6.1 μ (1639 cm^{-1}) – the  bond; at 7.6 μ (13.16 cm^{-1}) – the group $-CH-$; at 7.0 μ (1429 cm^{-1}) – the $-CH_2-$ group and no definite indications of the presence of the CH_3- group.

On the basis of the analysis data and the increased specific viscosity of the solid product from the condensation of polyvinyl alcohol with benzene in the presence of $AlCl_3$, we may consider the condensation product as having the approximate formula



$$\begin{array}{l}-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-\underset{\displaystyle \underset{\displaystyle CH_3-CH-CH_2-CH(OH)-}{\underset{|}{C_6H_4}}}{\underset{|}{CH}}-CH_2-CH{=}CH-\underset{\displaystyle C_6H_5}{\underset{|}{CH}}-\end{array}$$

SUMMARY

1. The reaction of benzene with polyvinyl alcohol in the presence of phosphoric acid was investigated. It was established that the reaction gave arylated products. The number of phenyl groups introduced depended on the duration of the reaction and the amount of catalyst.

2. The reaction of benzene with polyvinyl alcohol in the presence of $AlCl_3$ was investigated. 1,3-Diphenylpentane was isolated from the liquid reaction products and characterized. It was established that in the presence of $AlCl_3$ the hydroxyl groups of polyvinyl alcohol are partially substituted by phenyl rings. The destructive phenomena increased on increasing the amount of catalyst and the duration of the reaction.

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Received December 24, 1956

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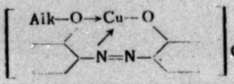
INTERNAL COMPLEX SALTS OF AZO COMPOUNDS

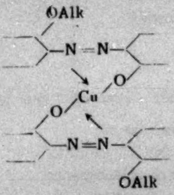
V. COPPERING OF o-HYDROXY-o'-ALKOXYAZO COMPOUNDS WITH SIMULTANEOUS DEALKYLATION

V. I. Mur

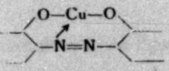
Previous reports [1] showed that depending on the conditions, o-hydroxy-o'-alkoxyazo compounds reacted with copper salts to give the following three types of complex.



(I)



(II)



(III)

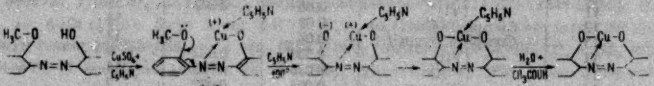
Complex (I) formed under the mildest conditions and was converted to complex (II) when treated with bases, even at room temperature; the latter was also prepared by reacting the initial azo compound with copper salts in the presence of ammonia. On heating o-hydroxy-o'-alkoxyazo compounds with copper sulfate in the presence of such organic bases as pyridine or ethanolamine, coppering occurred simultaneously with dealkylation, which gave complex (III); the same complex was prepared by reacting complex (I) with the given organic bases.

In the present work coppering of o-hydroxy-o'-methoxyazo compounds with simultaneous dealkylation was studied more closely to elucidate the role of complex formation in the dealkylation of these compounds and to determine if complexes (I) and (II) were intermediate compounds in this process. It also seemed interesting to trace the effect of substituents in the molecules of the o-hydroxy-o'-methoxyazo compounds on the capacity of the latter for dealkylation.

The study of this problem is not only of theoretical but also of practical value as the reaction studied is widely used for preparing direct azo dyes that are light-fast. However, in spite of the great number of patents [2], protecting copper complexes of o,o'-hydroxyazo dyes, and the methods of preparing them from the corresponding o-hydroxy-o'-methoxyazo dyes, we have not come across any information on the mechanism of coppering with simultaneous dealkylation. Although one paper [3] is devoted to the investigation of this reaction and a more thorough study was carried out on the effect of the conditions of treating o-hydroxy-o'-methoxyazo compounds with silver on their capacity for dealkylation, the nature of this reaction was not considered. The author's conclusions in this paper that the nitro group has no effect on dealkylation and that the sulfonic acid group hinders it cannot be considered sufficiently objective as comparisons were carried out under conditions that differed by more than one factor.

To elucidate the problems posed above, some o-hydroxy-o'-methoxyazo compounds and their copper complexes (I)and (II) were reacted with pyridine both in the presence and in the absence of copper salts and the degree of their dealkylation was determined. It was found that the starting azo compounds were not dealkylated, even when heated for a long time (40 hrs) at 100° with pyridine or a mixture of pyridine, ethyl alcohol and water. Their copper complexes (I) and (II) were dealkylated under even milder conditions. The methyl group of the azo compound was eliminated when the reaction was carried out in the presence of copper salts. It was observed that the dealkylation, occurring when o-hydroxy-o'-methoxyazo compounds were reacted with equivalent and somewhat greater amounts of copper sulfate and pyridine, proceeded practically at the same rate as in the case of the corresponding complexes (I) with the same amount of pyridine, under the given experimental conditions. In the presence of a smaller amount of copper sulfate the azo compounds were dealkylated much more slowly. Complex (II) dealkylates with greater difficulty under the same conditions; although the addition of copper salts did accelerate the process, its rate did not attain the value of the dealkylation of complex (I). A rise in temperature and an increase in the amount of pyridine promoted dealkylation. Depending on their nature, the substituents in o-hydroxy-o'-methoxyazo compounds either facilitated or hindered dealkylation; according to their effect on the capacity of an azo compound for dealkylation (under the given experimental conditions), the substituents in the position para to the methoxyl group may be arranged in the following order: $NO_2 > H > OCH_3 > CH_3 > Cl$. A nitro group, located in the position meta to the methoxyl, hindered dealkylation. In all cases the color of the solution deepened before dealkylation.

The data obtained, together with the results of the previous investigation [1] on the reactions of the complexes, indicate that in the presence of pyridine or ethanolamine coppering of o-hydroxy-o'-methoyazo compounds with simultaneous dealkylation proceeded analogously to the dealkylation of complex (I), according to the following scheme:



(IV)

Apparently complexes (I) and (II) are not intermediate stages in this reaction.

The formation of complex ion (IV) apparently explains the capacity of o-hydroxy-o'-methoxyazo compounds for dealkylation in the presence of copper salts and pyridine or other similar organic bases. Due to the copper atom attracting electrons from the nitrogen atom of the azo group, there is a displacement of electrons in this direction from the oxygen of the alkoxyl group and, as a result, the electron density of the oxygen decreases and the bond with the alkyl is weakened.

The data on the effect of substituents on the dealkylation capacity of azo compounds agree with the scheme proposed for this process. The nitro group in the position para to the alkoxyl, as an electronegative substituent affecting the chain of conjugated double bonds, attracted electrons from the oxygen atom and this weakened its bond with the alkyl and facilitated dealkylation. In the case of electron donor substituents, the reverse should happen and this actually occurred: methyl and methoxyl groups, in the position para to the alkoxyl, made dealkylation more difficult. A similar effect of a nitro group, in the position meta to the alkoxyl, and consequently in the position para to the azo group, was probably due to its attracting the electrons from the nitrogen atom of the azo group that was coordinated with the copper atom and this weakened the complex formation effect which affected the stability of the oxygen—alkyl bond.

EXPERIMENTAL

For the investigation we used anisole-(2-azo-1)-naphthol-(2) (V), (4-nitroanisole)-(2-azo-1)-naphthol-(2) (VI), (5-nitroanisole)-(2-azo-1)-naphthol-(2) (VII), (4-methoxyanisole)-(2-azo-1)-naphthol-(2) (VIII), (4-methylanisole)-(2-azo-1)-naphthol-(2) (IX) and (4-chloroanisole)-(2-azo-1)-naphthol-(2) (X), which were prepared by the usual method. Copper complexes of them with the composition 1 : 1 and 1 : 2 were prepared under the conditions adopted previously [1]. The new compounds were identified by analysis data and those described in the literature, by their melting points.

Reaction of azo compounds with pyridine. A solution of 0.5 g of the azo compound in 20 ml of pyridine in some experiments and in 50 ml of ethyl alcohol, 12.5 ml of pyridine and 1 ml of water in others was heated on a boiling water bath for 40 hrs, then the reaction mixture poured into 400 ml of water and the precipite which formed filtered off, washed with water and dried at 80°. The melting points of the substances obtained and the starting azo compounds were close; mixed samples of them melted practically without depression.

Reaction of copper complexes (I) and (II) of azo compound (V) with pyridine. A solution of 0.5 g of complex in 15 ml of pyridine in some experiments (a) and in 50 ml of ethyl alcohol, 5 ml of pyridine and 1 ml of water in others (b) was heated under reflux on a boiling water bath for 1 hr, then the reaction mixture quantitatively transferred into 400 ml of cold water and neutralized with acetic acid (to litmus) and the coagulated precipitate filtered into a tared Schott No. 2 funnel, washed with water until the smell of pyridine disappeared and dried to constant weight at 80°. The methoxyl group content of the substance obtained was determined by the Zeisel method and the percent of demethylation calculated.

Expt. no.	Designation of substance tested	Used in reaction (mole)		% demethylation found
		pyridine	$CuSO_4$	
1	(V)	0.028	0.002	16
2	(V)	0.028	0.0024	16
3	(V)	0.08	0.002	30
4	(V)	0.08	0.001	12
5*	(V)	0.2	0.002	83
6**	(V)	0.028	0.002	28
7	Complex (I) from (V)	0.08	0.002	32
8	Complex (II) from (V)	0.08	—	6
9	The same	0.08	0.001	13
10	(VI)	0.028	0.002	25
11	(VI)	0.08	0.002	55
12	Complex (I) from (VI)	0.08	—	54
13	Complex (II) from (VI)	0.08	—	12
14	(VII)	0.028	0.002	9
15	(VIII)	0.028	0.002	14
16	(IX)	0.028	0.002	7
17	(IX)	0.08	0.002	13
18	(IX)	0.14	0.002	19
19	Complex (I) from (IX)	0.028	—	6
20	Complex (II) from (IX)	0.028	—	1
21	(X)	0.028	0.002	6

* In Expt. 5, the reaction was performed without alcohol.

** In Expt. 6, cellosolve was used instead of alcohol.

The methoxyl group content in grams, found in the total amount of substance isolated (a), divided by the amount of starting material in grams (b) and multiplied by 100, corresponds to the percent methoxyl group content after demethylation. The ratio of the difference between the percent methoxyl group content of the starting material (c) and that obtained after dealkylation to the percent methoxyl group content of the starting material expresses the degree of demethylation. The value of the latter, multiplied by 100, corresponds to the percent of demethylation (x). After rearranging the equation obtained as a result of the above reasoning, the percent of demethylation may be calculated by the formula

$$x = 100\left(1 - \frac{100a}{b \cdot c}\right).$$

When the reaction was carried out under the conditions of experiment "a", complexes (I) and (II) of dye (V) were demethylated 80 and 45%, respectively, and under the conditions of experiment "b", 38 and 8%.

Reaction of azo compounds and their copper complexes (I) and (II) with copper sulfate and pyridine. To a hot solution of 0.002 mole of the azo compound or complex (I) or 0.001 mole of complex (II) in a definite amount of pyridine and 60 ml of ethyl alcohol was added a solution of the appropriate amount of copper sulfate in 1 ml of water and the reaction was performed and the substances obtained isolated and analyzed under the conditions of the previous experiment. The data from the experiments, carried out under these conditions with different compounds and amounts of reagents, are given in the table; in each case, the value of the percent of demethylations is the average result from two or three determinations.

SUMMARY

1. It was shown that dealkylation proceeded just as readily in reacting o-hydroxy-o'-methoxyazo compounds with an equivalent amount of copper sulfate and pyridine as in the corresponding complexes with a 1 : 1 composition, with the same amount of pyridine, all other conditions being equal; complexes with a 1 : 2 composition were more difficult to dealkylate.

2. It was found that, according to their effect on the dealkylation capacity of an azo compound reacted with copper sulfate and pyridine, substituents in the position para to the methoxyl group of o-hydroxy-o'-methoxyazo compounds may be arranged in the order: $NO_2 > H > OCH_3 > CH_3 > Cl$; a nitro group in a position meta to the methoxyl hinders dealkylation.

3. A scheme was put forward for the coppering of o-hydroxy-o'-alkoxyazo compounds with simultaneous dealkylation, which occurred when these compounds were reacted with copper salts and pyridine or other similar organic bases.

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Received March 5, 1957

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* Original Russian pagination. See C. B. translation.

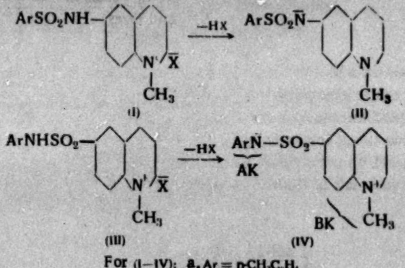
DIPOLAR IONS, FORMED BY THE ELIMINATION OF A PROTON FROM AN NH GROUP

XII. DERIVATIVES OF 6-QUINOLINESULFONIC ACID

A. M. Simonov

A study of quinoline salts, in particular the phenomenon of color in a series of these compounds, is of considerable interest as some representatives of this class are starting materials for the synthesis of dyes. In this work we studied the properties of quinolinium salts with a substituted sulfonamide group in the quinoline nucleus and the dipolar ions formed from them.

It was shown in previous reports [1] that quinolinium salts, containing an arylsulfamino group, may be converted to dipolar ions (betaines) by abstracting a proton from the NH group. Thus, for example, when treated with an aqueous ammonia solution, the methyl-p-toluenesulfonate of 6-p-toluenesulfamoquinoline (Ia) was converted into an orange dihydrate of 6-p-toluenesulfamoquinoline methylbetaine, which readily lost 2 molecules of water to form the anhydrous dipolar ion (IIa), which was bright red. The ease with which the quinolinium salt (Ia) was converted to a betaine was due to the NH group being affected by two systems possessing strong electron acceptor properties (the arylsulfonyl radical and the N-alkylquinolinium group).



For (I–IV): a. Ar = p-$CH_3C_6H_4$
b. Ar = p-$NO_2C_6H_4$
X = p-$CH_3C_6H_4SO_3$

As this work shows, the methylbetaine (IIb), containing a p-nitrobenzenesulfonyl radical, was formed even more readily from the quaternary salt than (IIa), under the action of pyridine; the higher lability of the hydrogen in the NH group, apparently, should be explained by an increase in the electron acceptor properties of the arylsulfonyl radical due to the introduction of a nitro group into it.

In order to study the effect of the onium N-atom on the lability of the NH group hydrogen, it seemed interesting to compare the properties of quinolinium salts I (a, b) with those of compounds isomeric to them, III (a, b), formed by melting methyl p-toluenesulfonate with anilides of 6-quinolinesulfonic acid. The quinoline nucleus in salts of structure (III) is connected to the NH group through an SO$_2$ group and as a result the onium N atom may affect the increase in lability of the NH hydrogen only by strengthening the electron acceptor properties of the acyl group.

One would expect that salt (IIIb) should, nevertheless, be readily converted into dipolar ion (IV b) as the NH group is affected by highly electrophilic groups – the p-nitrophenyl group and the acyl of the 6-quinolinesulfonic acid, whose electron acceptor properties are strengthened by the conversion of the N atom to the onium state. According to this hypothesis, betaine (IV b) is formed from the starting salt under the same conditions (treatment with bases that were equally weak) as the isomeric betaine (IIb).

On the contrary, the observation that the quinolinium salt (III a) was converted into a dipolar ion almost as readily as salt (I a) was very unexpected. Although the NH group in this compound, in contrast to salt (I a), was connected to only one strongly electrophilic radical, the effect of this radical on the NH group was so considerable that treatment of the onium salt even with a weak base (ammonia) resulted in the elimination of a proton and the formation of a dipolar ion (IV a).

Thus, isomeric salts with structures (I) and (III) reacted in the same way in weakly alkaline media. However, the reaction proceeded differently with caustic alkalis. In this case salt (I) was converted to a dipolar ion. However, if a hot aqueous solution of a salt with structure (III) was treated with excess caustic alkali, a betaine was not formed: the solution which was at first bright orange, gradually lost color and, after the excess alkali had been neutralized with acetic or dilute hydrochloric acid, it formed a precipitate that did not dissolve in excess acid and was slightly colored by impurities. Apparently this substance was a derivative of 1-methylquinoline. One could assume that the onium salt (III) was converted into a pseudo-base in a strongly alkaline medium; this conversion would be facilitated by the action of the $ArSO_2NH$ group, which would strengthen the effect of the onium N atom on the pyridine nucleus (cf. [2]). The pseudo-base remained in solution (due to the presence of the sulfamide group) and was oxidized by atmospheric oxygen to quinolone. We had observed the formation of a pseudo-base instead of a dipolar ion previously when some benzimidazolium salts, containing an arylamino group, were treated with alkaline agents [3].

The properties of the isomeric dipolar ions with structures (II) and (IV) did not depend noticeably on the order of connection of the $-SO_2N-$ group to the benzene and quinoline nuclei: the betaines (IV), like compounds (II) which are isomeric to them, dissolve in dilute acetic acid, are not hydrated when kept in water vapor and are brightly colored (dipolar ions (IIa) and (IVa) are bright red, (IIb) and (IVb) are bright yellow). According to the hypotheses put forward earlier, the strong deepening of the color in going from an onium salt to a dipolar ion is due to the formation in the molecule of a strongly electron donating chromophore,* an azeniate N atom (bonded dicovalently and with a negative charge) which has an effect when the molecule contains an electrophilic chromophore group (methinimonium, nitro group, quinoid nucleus, etc.) [5]. It should be noted that betaines (IV a) and (IV b) have almost the same deep color as compounds (IIa) and (IIb) although here the azeniate N atom is not conjugated with the electrophilic chromophore system (the methylquinolinium group). The deep color of these compounds may be explained on the basis of the investigations carried out by Izmail'skii and Solodkov on the color of molecular complexes of quinolinium salts with aromatic amines and amines of the quinoline series [6]. All these complexes have a deep color, which according to the authors is due to intermolecular reaction of the chromophore systems. Apparently, the color of betaines (IV) should also be explained by intermolecular reaction of separate electrophilic (BK) and electron donor (AK) components, included in the molecules of these compounds. It is nevertheless possible to conclude from a comparison of the color of betaines with structures (II) and (IV) that in considering the color phenomena in the series of dipolar ions containing conjugated chromophore systems, the possibility of intermolecular reaction in these systems, especially in crystalline compounds, should also be taken into account.

EXPERIMENTAL

6-p-Nitrobenzenesulfamoquinoline. This compound was prepared by the reaction of 6-aminoquinoline with p-nitrobenzenesulfonyl chloride in pyridine solution. The almost colorless, rectangular plates (from alcohol) had m. p. 227°.

Found %: S 9.68. $C_{15}H_{11}O_4N_3S$. Calculated %: S 9.74.

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* See [4] for V. A. Izmail'skii's classification of chromophore systems.

Methyl p-toluenesulfonate of 6-p-nitrobenzenesulfamoquinoline (Ib). The yellowish white crystals (from dilute alcohol) had m. p. 264-265° (with decomp.). The salt was converted into a betaine by adding to it an aqueous solution of ammonia, pyridine or excess sodium acetate.

Found %: S 12.34. $C_{23}H_{21}O_7N_3S_2$. Calculated %: S 12.44.

Methylbetaine of 6-p-nitrobenzenesulfamoquinoline (IIb). The compound was prepared by adding a small excess of ammonia to a hot (80°) aqueous solution of the quaternary salt. The dark yellow precipitate was washed with water and dried in a desiccator over sodium hydroxide. The betaine was insoluble in dioxane, acetone and chloroform, difficultly soluble in alcohol and in hot nitrobenzene and pyridine but readily soluble in a mixture of pyridine and water, from which it crystallized as bright yellow needles; it also dissolved in dilute acetic acid. It was not hydrated in water vapor. The decomposition point of the betaine was at about 280°.

Found %: S 9.31, 9.35. $C_{16}H_{13}O_4N_3S$. Calculated %: S 9.34.

6-Quinolinesulfonyl chloride. 4 g of 6-quinolinesulfonic acid, dried at 110-120°, was heated with an equimolecular amount of phosphorus pentachloride (4 g) for 2 hrs at 110-120°. The mixture was cooled and then treated simultaneously with ice and an ice-cooled 10% solution of soda. The filtrate was sucked off and the acid chloride dissolved in benzene. The benzene solution was washed with soda solution and dried with calcium chloride. The benzene was distilled off and the residue recrystallized from low-boiling benzine. The snow-white crystals had m. p. 88.5-89°. The compound rapidly decomposed with hot water to form a clear solution.

Found %: Cl 15.36; S 13.95. $C_9H_6O_2NSCl$. Calculated %: Cl 15.57; S 14.05.

p-Toluidide of 6-quinolinesulfonic acid (6-N-p-tolylsulfamidoquinoline). The 6-quinolinesulfonyl chloride was added to a solution of an equimolecular amount of p-toluidine in dry pyridine. The following day, the solution was poured into water. The precipitate was carefully washed with hot water and recrystallized twice from dilute alcohol. The colorless crystals were soluble in dilute sodium hydroxide solution. The m. p. was 189.5-190°.

Found %: S 10.67. $C_{16}H_{14}O_2N_2S$. Calculated %: S 10.75.

Methyl p-toluenesulfonate of 6-[N-(p-tolyl)-sulfamido]-quinoline (IIIa). The yellowish white crystals (from a mixture of alcohol and ether) had m. p. 220-222° (with decomp.).

Found %: S 12.99. $C_{24}H_{24}O_5N_2S_2$. Calculated %: S 13.23.

When a concentrated aqueous solution of the salt was treated with a small excess of ammonia, the solution became red-orange and a precipitate of orange needles of the betaine was formed on standing. The addition of alkali to a hot aqueous solution of the salt gave a red-orange solution, whose color rapidly paled. If this solution, which had a pale pink color due to traces of side products, was neutralized with acetic acid or treated with an excess of ammonium chloride, a pale pink precipitate was formed, which was readily soluble in alkalis, acetone and pyridine and almost insoluble in dilute acids. This product, which was not examined more closely, was apparently a 1-methylquinoline derivative.

Methylbetaine of 6-[N-(p-tolyl)-sulfamido]-quinoline (IVa). Ammonia was added dropwise to a hot solution of 0.48 g of the quaternary salt in 8 ml of water until there was a faint smell. The red-orange precipitate formed was sucked off, carefully washed with water and dried in a desiccator over alkali. The bright red lustrous crystals (needles) became orange in color when ground up. The yield was 0.23 g. The betaine was soluble in dilute acetic acid and insoluble in pyridine. The product was recrystallized from 90% acetic acid; it melted at about 235° (with decomp.). The betaine was not hydrated on standing in water vapor.

Found %: S 10.26, 10.15. $C_{17}H_{16}O_2N_2S$. Calculated %: S 10.26.

p-Nitroanilide of 6-quinolinesulfonic acid. The compound was prepared by reacting p-nitroaniline with 6-quinolinesulfonyl chloride in pyridine. The colorless crystals (from alcohol) with m. p. 242-243°, were soluble in dilute alkali and an aqueous solution of ammonia to give a yellow color.

Found %: S 9.70. $C_{15}H_{11}O_4N_3S$. Calculated %: S 9.74.

Methyl p-toluenesulfonate of 6-[N-(p-nitrophenyl)-sulfamido]-quinoline (IIIb). The pale yellow crystals (from dilute alkali) had m. p. 266-267°.

Found %: S 12.32. $C_{23}H_{21}O_7N_3S_2$. Calculated %: S 12.44.

When the salt was treated with ammonia (slight excess), soda or pyridine, it was converted into the betaine. Treatment of a solution of the quaternary salt with sodium hydroxide did not give a dipolar ion: the originally orange solution became yellow and, on acidification, deposited a pale colored precipitate, which was almost insoluble in excess acid.

Methylbetaine of 6-[N-(p-nitrophenyl)-sulfamido]-quinoline (IV b). A hot solution of 0.52 g of the quaternary salt in 12 ml of 40% alcohol was treated with a slight excess of ammonia. Cooling the solution yielded a yellow precipitate (0.32 g), which was recrystallized from dilute alcohol and dried in a desiccator over phosphorus pentoxide. The fine yellow needles were soluble in dilute acids and in hot nitrobenzene and difficultly soluble in acetone and pyridine. The melting point, depending on the rate of heating, lay between 237 and 245°. The compound was not hydrated on standing in water vapor.

Found %: S 9.33, 9.29. $C_{16}H_{13}O_4N_3S$. Calculated %: S 9.34.

SUMMARY

1. Quinolinium salts, of structure (III a, b), which are 6-quinolinesulfonic acid derivatives, were synthesized. It was shown that treatment of these salts with weakly alkaline agents eliminated a proton from the NH group and gave dipolar ions as in the case of isomeric salts (I).

2. It was established that quinolinium salts (III), in contrast to (I), were not converted to betaines by treatment with excess caustic alkali.

3. The reasons for the color of dipolar ions with structure (IV) were discussed.

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Received March 18, 1957

All-Union Correspondence Institute of the Textile
and Light Industries

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* Original Russian pagination. See C. B. translation.

** In Russian.

CONDENSATION OF 6-QUINOLINEALDEHYDE WITH KETONES AND ESTERS

B. P. Lugovkin

In developing our previous work on the study of the chemical properties of 6-quinolinealdehyde [1] we investigated its condensation with ketones and some esters.

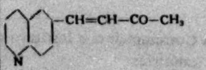
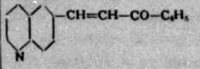
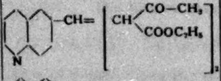
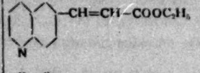
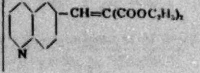
By reacting the aldehyde with acetone in a dilute aqueous alkaline solution we were able to obtain quinolidene-(6)-acetone (I) in 33% yield. A high polymer product was prepared in an alcohol solution in the presence of sodium ethoxide.

The aldehyde reacted readily with acetophenone in the presence of sodium ethoxide. This gave a 71% yield of quinolidene-(6)-acetophenone (II).

The aldehyde was reacted with acetoacetic ester in the presence of pyridine with cooling of the reaction mixture [2]. Only the diethyl ester of quinolene-(6)-bis-acetoacetic acid (III) could be isolated from the reaction products in a 33% yield. The aldehyde condensed with ethyl acetate to give ethyl quinolyl-(6)-acrylate (IV) in 22% yield.

The condensation product of the aldehyde with diethyl malonate was identified as the methiodide of diethyl quinolidene-(6)-malonate (V). The ester yield was 49%.

Condensation of the aldehyde (2 moles) with diethyl succinate in the presence of sodium ethoxide and piperidine did not give diethyl α,δ-diquinolyl-(6,6')-fulgenate [2].

Expt. no.	Formula	Condensation product			Methiodide		
		melting point	N (in %)		melting point	Iodine (in %)	
			found	calc.		found	calculated
I		112–112.5°	6.83	7.10	236–237°	37.62	37.43
II		146–146.5	5.74	5.40	245–247	31.59	31.64
III		151–152	3.98	3.50	195–196	23.30	23.45
IV		Thick liquid	5.82	6.16	202–204	34.02	34.39
V		Thick liquid	–	–	182–184	28.40	28.77

EXPERIMENTAL

All the experiments required anhydrous 6-quinolinealdehyde (m. p. 75-76°).

Condensation with acetone.* 3 ml of 2 N sodium hydroxide solution was added to 4 g of the aldehyde and 8 g of acetone in 200 ml of water. The mixture was kept for 48 hrs (with periodic shaking) and then the thick liquid produced was extracted with chloroform. Drying with sodium sulfate and removal of the solvent yielded 4.2 g of a solid residue. Extraction of the mixture with benzine (13 ml) and benzene (2 ml) gave 1.66 g of crystals with m. p. 111-112° (a tarry product was left in the sleeve). A second recrystallization produced light yellow crystals. The substance was readily soluble in organic solvents, difficultly soluble in light benzine and dissolved in warm water. The picrate had m. p. 180° (from glacial acetic acid).

The phenylhydrazone consisted of yellow crystals with m. p. 169° (recrystallized from benzene).

Found %: N 14.68. $C_{19}H_{17}N_3$. Calculated %: N 14.63.

Methiodide. When 0.3 g of the substance and 0.6 ml of methyl idodide were kept for 3 days, they yielded 0.37 g of dark yellow crystals (after washing with hot anhydrous alcohol). The substance dissolved when heated in water, with great difficulty in alcohol and was insoluble in ether.

Condensation with acetophenone. A solution of sodium ethoxide (0.5 g of metallic sodium in 10 ml of alcohol) was added to 5 g of aldehyde and 4.3 g of acetophenone in 5 ml of anhydrous alcohol; the temperature rose to 27° and a crystalline product rapidly separated. After dilution, washing with water and recrystallization from alcohol, the product yielded 5.86 g of crystals with m. p. 145-146°. The substance was recrystallized from benzene. It dissolved readily in alcohol and benzene on heating, with difficulty in ether and was insoluble in water. The picrate had m. p. 233° (from glacial acetic acid).

The phenylhydrazone formed light yellow crystals with m. p. 178° (recrystallized from dioxane).

Found %: N 11.89. $C_{24}H_{19}N_3$. Calculated %: N 12.03.

Methiodide. From 0.5 g of the substance and 1 ml of methyl iodide (under the conditions of the previous experiment) we obtained 0.6 g of yellow crystals (after washing with hot, anhydrous alcohol). The product dissolved in water on heating, with great difficulty in alcohol and was insoluble in ether.

Condensation with acetoacetic ester. A solution (−5°) of 0.5 g of piperidine in 2 ml of anhydrous alcohol was added to 5 g of aldehyde** and 4.3 g of ester at −5°. The mixture was kept in the cold (on the average 0-5°) for 48 hrs and washed with cold and then hot water to give a thick liquid, which crystallized on standing. Recrystallization from benzene (5 ml) with cooling, yielded 2.2 g of crystals with m. p. 146°, which formed white microcrystals after a second recrystallization. The substance dissolved in alcohol, benzene and dioxane on heating. The picrate had m. p. 185-186° (from glacial acetic acid).

Methiodide. By heating 0.3 g of the substance with 0.5 ml of methyl iodide on a water bath for 0.5 hours, we obtained 0.25 g of light yellow crystals (recrystallized from anhydrous alcohol). They dissolved in water with heating, in alcohol with difficulty and were insoluble in ether.

Condensation with ethyl acetate. To a solution of ethyl sodioacetate, prepared from 0.95 g of metallic sodium in 20 g of ester, cooled in snow, was added a cooled solution of 6.4 g of aldehyde in 9 g of ester. The mixture was kept at room temperature for 1 hr and then 5 ml of glacial acetic acid was added followed by water until the ester layer had separated completely. After removal of the solvent, the residue was vacuum distilled. A fraction with b. p. 153-186° (1 mm) isolated was redistilled; we obtained 2 g of a very thick liquid with b. p. 198-201° (6-7 mm), $n^{20}D$ 1.6369, d^{20}_{20} 1.0641. The picrate had m. p. 238-239° (from glacial acetic acid).

Methiodide. By heating 0.25 g of the substance with 0.5 ml of methyl iodide on a water bath for 0.5 hrs, we obtained 0.35 g of golden yellow crystals (recrystallized from anhydrous alcohol). They dissolved in water, in alcohol on heating and were insoluble in ether.

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* Condensations under other conditions did not lead to the desired results; in every case, tarry products were obtained.

** Compound (III) required 2.59 g of aldehyde.

Condensation with diethyl malonate. 0.5 g of piperidine was added to 4 g of aldehyde and 4.08 g of ester; the temperature rose to 16°. After standing for 48 hrs, the mixture was heated on a water bath for 2 hrs. The product was washed with hot water and dried in ether solution with sodium sulfate to yield 7.4 g of an oily liquid, which did not distill in vacuum (4 mm). The picrate had m. p. 196-198° (from glacial acetic acid).

Methiodide. By keeping 1.08 g of the substance and 1.5 ml of methyl iodide for 3 days, we obtained 0.8 g (which corresponds to 3.71 g of ester) of dark yellow crystals (recrystallized from anhydrous alcohol with active charcoal). They dissolved in water and alcohol with heating and were insoluble in ether.

SUMMARY

6-Quinolinealdehyde was condensed with acetone, acetophenone, acetoacetic ester, ethyl acetate and diethyl malonate. The condensation products were characterized as methiodides.

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Received April 5, 1957

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* All-Russian Central Union of Consumers' Societies.

** Original Russian pagination. See C. B. translation.

*** In Russian.

REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

IX. REASONS FOR THE COLOR OF DIAZONIUM SALTS OF ARYLSULFAMIC ACIDS

D. Z. Zavel'skii and L. A. Lishnevskaia

In a previous report [1] it was shown that diazonium chlorides undergo salt exchange with the sodium salts of arylsulfamic acids, to form diazonium salts of arylsulfamic acids:

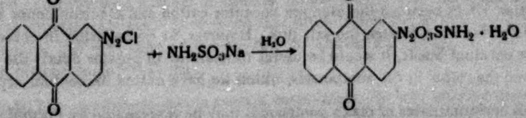
$$\mathrm{Ar{-}N_2Cl + NaO_3SNH{-}Ar' \longrightarrow Ar{-}N_2O_3SNH{-}Ar' + NaCl}$$

When an electron acceptor substituent is present in the benzene nucleus of the diazo cation, these salts crystallize well from aqueous solutions and, in the solid form, are deeply colored from golden yellow and red to almost black. It was established that the more electronegative the substituents in the benzene nucleus of the diazo cation and the higher their capacity for electron attraction, the less water-soluble were the corresponding arylsulfamates and the deeper their color. The color also deepened on introducing electron donor substituents into the benzene nucleus of the arylsulfamic acid.

Diazonium arylsulfamates, deeply colored in the solid state, dissolved in water to form much lighter and weaker colored solutions. A study of the absorption spectra of aqueous solutions of various concentrations showed that they did not follow the Lambert-Beer law due to dissociation of the arylsulfamates into the colorless ions forming them.

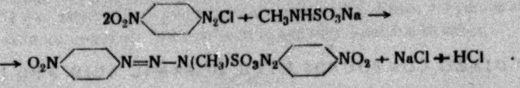
The properties of diazonium arylsulfamates which are quite unusual in comparison with most other diazonium salts, induced us to attack the problem of what there was exactly in the structure of arylsulfamic and, in particular, phenylsulfamic acids, which caused the deep color of their diazonium salts. First of all, it was interesting to determine whether the unsubstituted acid itself or its alkyl derivatives were capable of giving colored diazonium salts, i. e., did the phenyl nucleus of phenylsulfamic acid have a definite role.

A series of control experiments showed that diazo compounds of the benzene series reacted with unsubstituted sulfamic acid in an acid medium to give colorless solutions from which solid salts could not be isolated. Prolonged research established that 2-anthraquinonyldiazonium chloride, which itself was golden yellow, reacted with the sodium salt of sulfamic acid to give crystalline 2-anthraquinonyldiazonium sulfamate.



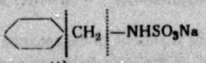
The structure of this salt, containing one molecule of water of crystallization was established by quantitative coupling with β-naphthol (giving the diazo component content), titration with nitrite (sulfamic acid content) and diazo nitrogen determination. It was found that 2-anthraquinonyldiazonium sulfamate had the same golden yellow color as the chloride. Consequently, the relatively weak color of the salt depends not on the nature of the anion but on the nature of the diazo cation, containing the anthraquinone ring. That means that unsubstituted sulfamic acid is incapable of giving salts of deep color with diazo compounds.

We previously studied [2] the reaction of methylsulfamic acid with diazo compounds in an acid medium. It was established that methylsulfamic acid did not form salts of the $ArN_2O_3SNHCH_3$ type under these conditions but underwent diazoamino condensation with nitrodiazobenzene and 2,5-dichlorodiazobenzene, to precipitate diazonium salts of methylaryltriazene-N-sulfonic acids, which crystallized readily.



These salts are colored from light yellow to yellow in the case of p-, m- and o-nitrodiazobenzene and in the case of 2,5-dichlorodiazobenzene, the salt first precipitates as colorless needles, which gradually changed into yellow cubes. Consequently, methylsulfamic acid, even substituted with a nitrophenylazo radical (containing a chromophore), is incapable of giving deeply colored salts with aryldiazo cations.

One may conclude from this that the formation of deeply colored diazo salts occurs only when the sulfamic group is connected directly to the conjugated system of the benzene nucleus. To confirm this conclusion we synthesized the sodium salt of benzylsulfamic acid in which the benzene ring is separated from the sulfamic group by a methylene bridge (A).



(A)

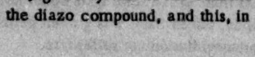
It was found that in a mineral acid medium, benzylsulfamic acid was incapable of precipitating salts with diazo compounds and instead the free acid itself separated from the solution. Such behavior may be explained by the fact that benzylsulfamic acid is a much weaker acid than phenylsulfamic acid, as the ionization constant at 25° is equal to $3.0 \cdot 10^{-10}$ for aniline and $2.4 \cdot 10^{-5}$ for benzylamine. When the salt exchange was carried out in an acetic acid medium instead of a mineral acid one, crystalline 4- and 3-nitrophenyldiazonium benzylsulfamates could be isolated and both were light yellow in color.

Acetic acid solutions of 4-chloro-, 2-nitro- and 4-nitro-2-methylphenyldiazonium did not form solid benzylsulfamates, apparently due to their ready solubility and the reaction solutions were colorless. Under those conditions, 2,5-dichloro- and 4-nitro-2-chlorodiazobenzene also formed light yellow, but unstable diazo salts which were rapidly converted into diazoamino compounds and tar.

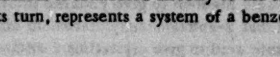
It was established that the separation of the sulfamic group from the benzene ring using, for example, a methylene bridge, as occurs in benzylsulfamic acid, breaks down the mechanism which brings about the deep color of the diazonium salts of arylsulfamic acids. In other words, the bathochromic effect in such salts is observed only when the conjugated system of the benzene nucleus is connected directly to the sulfamic group which forms a salt link with the diazo compound, and this, in its turn, represents a system of a benzene ring, connected to a diazo group.

It has already been noted that by increasing the electronegativity of the substituent in the benzene nucleus of an arylsulfamic acid, one can obtain gradually deeper and deeper colored salts. It is logical to assume from this that the conjugation effect between the electron acceptor cation and electron donor anion, without which color is impossible, is transmitted through the salt link. However, as conjugation in colored organic bodies is realized only through covalent bonds, it would be useful to examine in greater detail the character of the bond between the cation and the anion in the compounds, which we have called diazonium arylsulfamates.

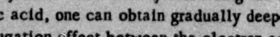
The structure of arylsulfamates of diazo compounds may be represented by Formulas (I)-(IV).



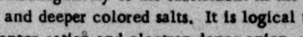
(I)



(II)

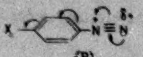


(III)



(IV)

In Formula (I) the bond between the ions may, at first glance, be considered as purely electrovalent, characteristic of quaternary nitrogen salts. However, due to the free electron pair of the terminal nitrogen, there is conjugation in the diazonium cation which results in the formation of a fractional positive charge on the terminal nitrogen atom and in a corresponding decrease in the positive charge of the second nitrogen (B).



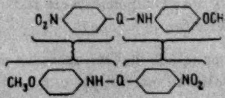
(B)

The more electronegative the substituent X, the lower the electron density at the terminal nitrogen and the greater the similarity of the structure of the salt to Formula (III). However, the salts of strong mineral acids with diazo compounds have a structure which is much more accurately described by Formula (I). L. V. Grachev [3], who arrived at the same conclusion by studying the properties of diazo compounds by potentiometric titration of their aqueous solutions with a glass electrode, found that the pH value of 4-nitrophenyldiazonium chloride equals 5.6. The pH values we measured for 4-nitrophenyldiazonium phenyl- and 4-tolylsulfamates [1] were found to be the same and equal to 5.7. The closeness of the pH values of chlorides and arylsulfamates of diazo compounds indicates that the latter, too, should be assigned the diazonium formula (I). This formula is also supported by the fact that the arylsulfamates of diazo compounds are formed as a result of exchange between diazonium chlorides and sodium arylsulfamates in a mineral acid medium and that they are readily soluble in water and dissociate into the original colorless ions. Formula (II) should be rejected as it contains pentacovalent nitrogen, and Formula (IV) is unsuitable as it assumes a covalent bond between the ions.

As is known, the modern theory on color of organic compounds holds that color, i. e., the displacement of light absorption towards the long wavelength part of the spectrum, is due to the presence in the organic compound of a system of conjugated double bonds which has at its ends electron donor and electron acceptor groups held together by a conjugated system with a tendency to form dipoles [4]. In the case of diazonium arylsulfamates, however, formed similarly to type (I), substituents X and Y are conjugated by a system which is interrupted by the salt link.

As is known, V. A. Izmail'skii and co-workers showed, as a result of extensive and thorough work [5], that with two conjugated systems with sufficiently strong electron acceptor and electron donor substituents at the ends, color may be observed even in substances in which the two systems are separated from each other by some group Q, incapable of conjugation. For example, while nitrobenzene and aniline are colorless, 4-nitrobenzylanilide [6] is yellow or orange in color (there are two forms) and 4-nitro-4'-methoxybenzylanilide is red [7].

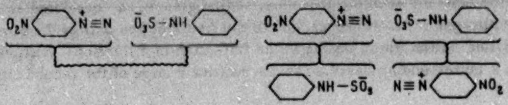
Izmail'skii considered that the reason for color in such bodies is an intermolecular reaction of the electron donor and the electron acceptor systems, which he represented in the following schematic form:



This type of reaction is known to occur between nitro compounds or quinones and arylamines, phenols, etc., and is being investigated carefully by a number of authors. In particular, Izmail'skii and other studied the reaction of nitrobenzene with dimethylaniline. They found that while nitrobenzene in a pyridine solution has λ_{max} 309 mμ and dimethylaniline 315 mμ, then p-nitro-N-dimethylaniline has λ_{max} 395 mμ and a solution of dimethylaniline in excess nitrobenzene – 430 mμ.

On this basis, Izmail'skii considered that in certain cases intermolecular reaction may play a very important part as a color factor in dyes.

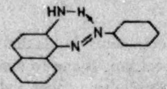
From the reasons given above one may suppose that the reaction of the arylsulfamate anion with a diazo cation in solution and in the crystalline form is also intermolecular according to the following scheme:



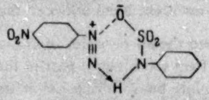
In this case salt formation only brings the electron donor and electron acceptor systems into sufficiently close proximity.

However, special experiments showed that on dissolving sodium phenyl- or tolylsulfamates in alcohol and diluting these solutions with nitrobenzene or dinitrochlorobenzene (electron acceptor systems), like acetanilide or benzenesulfonylsulfanilic acid ($C_6H_5NHSO_2C_6H_4SO_3H$), no deepening of color was noticed. Consequently, the reason for color in diazonium arylsulfamates is actually salt formation and not intermolecular reaction.

It is known that in o-aminoazo dyes there is a hydrogen bond between the amino group hydrogen and one of the nitrogens in the azo group, due to the unshared electron pair on the latter. Such a hydrogen bond, causing a definite change in the electron structure of the arylazo radical and the formation of an additional ring, is the reason for the deepening of color, especially when the hydrogen is substituted by a metal. Considering that the terminal nitrogen in a diazonium cation also has an unshared electron pair, we considered that a hydrogen bond could also form in diazonium arylsulfamates, which for the same reason would also cause a deepening in the color:



o-Aminoazo dye



4-Nitrophenyldiazonium salt of phenylsulfamic acid

To determine whether this hypothesis was correct, we synthesized N-ethylphenylsulfamic acid, which has not been described in the literature, by sulfonating N-ethylaniline with anhydropyridinesulfonic acid in pyridine. This arylsulfamic acid, in which the amino group hydrogen was substituted by an ethyl group gave salts with 4-chloro-, 3-nitro- and 4-nitrophenyldiazoniums, colored brownish-yellow, orange-red and reddish brown, respectively. A comparison of these salts with those synthesized earlier from the corresponding phenylsulfamates showed that the ethyl derivatives were only slightly ligther in color. The rest of the properties of diazonium ethylphenylsulfamates were also found to be quite similar to those of phenylsulfamates, the only difference being that they were somewhat less stable to storage in a dry form and to even slight heating in water. 2,5-Dichloro- and 2-chloro-4-nitrophenyldiazonium salts of ethylphenylsulfamic acid could not be prepared, as instead of them, water-insoluble products of diazo salts rearranging to diazoamino compounds were formed. The same result was obtained on reacting these diazoniums with phenyl- and tolylsulfamic acids [1].

From these experiments one may conclude that the presence of hydrogen on the amino group of an arylsulfamic acid results only in a certain stabilization and slight deepening of the diazo salt colors and that the substitution of hydrogen by the ethyl group does not interfere with the conjugation of the electron donor and electron acceptor systems, connected by the salt bond. Consequently, the main reason for color in diazonium arylsulfamates is the presence of a salt bond of a special character between its component ions and which is capable of transmitting the conjugation effect between the latter.

EXPERIMENTAL

Synthesis of sodium benzylsulfamate. Benzylamine was synthesized by the method of Ing and Manske [8]. The barium salt of benzylsulfamic acid was synthesized using Paal and Lowitsch's procedure [9]. The sodium salt of benzylsulfamic acid, which is not described in the literature, was prepared by the following method. A concentrated aqueous solution of 9.7 g of Glauber's salt was added to 15.3 g of barium benzylsulfamate. The reaction mixture was heated to 55-60° and the precipitate of barium sulfate filtered off and washed with a small amount of hot water. Cooling the combined filtrate and wash water in ice yielded a crystalline precipitate of sodium benzylsulfamate, which was separated by filtration. The rest of the sodium salt was obtained by evaporating the mother liquors. The pure product was obtained by recrystallization from alcohol.

Benzylsulfamic acid and its salts may be determined by nitrosation with nitrite in an acid medium.

0.2365 g of substance: 11.2 ml 0.1 N nitrite solution. $C_7H_8O_3NSNa$. Calculated: 11.3 ml of 0.1 N sodium nitrite solution.

Synthesis of sodium N-ethylphenylsulfamate. Technical monoethylaniline was freed from aniline and diethylaniline by the method of Blume and Kloffler [10], which gave good results. The purified monoethylaniline was sulfonated by the method described in a French patent [11] for monomethylaniline. By changing the method, it was possible to obtain an end product of good quality in high yield. 225 ml of pyridine was placed in a three-necked flask, fitted with a stirrer, a thermometer and a dropping funnel and externally cooled in an ice—salt mixture, and 64 g of chlorosulfonic acid was added dropwise at −10° at such a rate that the temperature did not rise above 5°. After the addition, the temperature of the mixture was allowed to rise to 20°, 60.5 g of ethylaniline added and the mixture heated for 2 hrs at 60-70°.

The mixture was cooled to 20°, poured into a suspension of soda in water and the pyridine removed by steam distillation. The residue in the flask was cooled, when it deposited a voluminous precipitate of coarse, brownish crystals. The precipitate was filtered off, washed first with water and then with alcohol and ether and dried. The yield was 88%.

After 2 recrystallizations from alcohol, it formed coarse white crystals with a hardly noticeable brownish tinge and a strong silky sheen.

Found %: Na 10.2. $C_8H_{10}O_3NSNa$. Calculated %: Na 10.3.

Reactions of benzylsulfamic acid with diazonium chlorides in a mineral acid medium. An aqueous solution of sodium benzylsulfamate, saturated at room temperature, was cooled in an ice bath. With vigorous stirring, concentrated hydrochloric acid solutions of phenyl-, 4-chlorophenyl-, 2,5-dichlorophenyl-, 4-nitrophenyl- and 4-nitro-2-chlorophenyldiazonium chlorides were added to this solution. The diazonium chloride solutions were prepared by the method described in the previous report [1].

In all cases, the solutions first obtained deposited colorless or pale yellow crystals — plates, which were readily soluble in water and coupled with azo components more or less vigorously. Analysis showed that the precipitate was free benzylsulfamic acid, containing a little diazonium compound.

Consequently, in a hydrochloric acid medium, benzylsulfamic acid, liberated from its sodium salt, is incapable of displacing hydrochloric acid from its aryldiazonium salts.

Reaction of sodium benzylsulfamate with diazonium acetates. A saturated solution of sodium acetate was added to a hydrochloric acid solution of a diazo compound until the pH reached 3-4. The acetic acid diazo solution obtained was added with cooling and stirring to an aqueous suspension of sodium benzylsulfamate.

4-Nitrophenyldiazonium salt of benzylsulfamic acid. When 4-nitrophenyldiazonium was added to a suspension of sodium benzylsulfamate, a voluminous, pale yellow precipitate of coarse, lustrous crystals was immediately deposited. Under a microscope the crystals appeared as broad tablets with bevelled edges. The precipitate was recrystallized from water heated to 60°. The recrystallized precipitate was brighter yellow in color as the crystals were bigger. It was washed with ice water, pressed out first on the filter and then on porous plate and dried in vacuum over solid alkali, spread out as a very thin layer. The diazo salt dissolved completely in cold water and coupled vigorously with azo components. When heated in the dry state it decomposed with an explosion.

Found %: N 16.49; S 9.25; diazo nitrogen 8.53. $C_{13}H_{12}O_5N_4S$. Calculated %: N 16.66; S 9.53; diazo nitrogen 8.33.

3-Nitrophenyldiazonium benzylsulfamate. An acetic acid solution of 3-nitrophenyldiazonium was poured into a concentrated solution of sodium benzylsulfamate and after 2-3 min, a light yellow precipitate formed. Under a microscope it appeared as elongated plates. The precipitate was filtered off, washed with ice—water, pressed out on a porous plate and dried in vacuum. The substance was almost completely soluble in water, coupled vigorously with azo components and decomposed with an explosion when heated in the dry form.

Found %: diazo nitrogen 8.49. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

Sodium benzylsulfamate and acetic acid solutions of diazobenzene and 4-chloro-, 2-nitro- and 4-nitro-2-methyldiazobenzenes. When acetic acid solutions of the diazo compounds listed were poured into thick suspensions of sodium benzylsulfamate, the color of the solutions did not change and no precipitates were formed.

Sodium benzylsulfamate and 4-nitro-2-chlorodiazobenzene. When the diazo solution was poured into a suspension of sodium benzylsulfamate, a light yellow precipitate formed immediately. We were unable to isolate it as it rapidly changed into an orange tar, which gradually reddened. The change was complete in a few minutes. The tar was almost insoluble in water and gave a weak reaction for active diazo compound. Attempts to stop the reaction at the formation of the diazo sulfamate were unsuccessful.

Sodium benzylsulfamate and 2,5-dichlorodiazobenzene. An acetic acid solution of the diazo compound was combined with a suspension of the benzylsulfamate. A light yellow precipitate gradually separated and under a microscope it appeared as needles. The filtered and washed precipitate was insoluble in water, but dissolved readily in glacial acetic acid. The addition of α-naphthylamine to the acetic acid solution and gentle heating produced an intense color, characteristic of diazo compounds.

Reaction of sodium N-ethylphenylsulfamate with diazonium chlorides. 4-Nitrophenyldiazonium N-ethylphenylsulfamate. When the diazo solution was added to a suspension of ethylphenylsulfamate, the reaction mixture acquired a red-brown color. The precipitate, which rapidly appeared, gradually increased. It consisted of coarse, brick red crystals with a gold luster, which appeared as broad plates under a microscope. The substance had all the properties of a diazonium salt; it was completely soluble in water, coupled readily with azo components in a neutral medium and decomposed with an explosion, when heated in the dry state.

We were unable to purify the substance by recrystallization as in contact with water heated to 50°, it immediately formed a tar. The diazo salt obtained was very unstable on storage. After several hours, even in vacuum, it decomposed, forming a liquid, tarry mass. For analysis we had to use an unpurified sample of the diazo salt, freshly precipitated and dried in vacuum on a porous plate.

Analysis for diazo component content. To a solution of a sample of the substance in cold water was added excess 0.1 N β-naphthol solution, adjusted to pH 7 by the addition of acetic acid. The solution was kept for 20 min and the excess β-naphthol then titrated with a 0.1 N solution of p-nitrophenyldiazonium.

0.7284 g of substance: 19.70 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_5N_4S$. Calculated: 20.74 ml of 0.1 N β-naphthol solution.

3-Nitrophenyldiazonium N-ethylphenylsulfamate. When the components were mixed, the mixture acquired a pale red color, which gradually became intense. Simultaneously, a lustrous orange-red precipitate formed. The filtered precipitate consisted of coarse orange-red plates, which were readily soluble in cold water and coupled with azo components readily.

The substance was so unstable that we were unable to recrystallize it from warm water.

Analysis for diazo component content: 0.6238 g of substance: 16.9 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_5N_4S$. Calculated: 17.8 ml of 0.1 N β-naphthol solution.

4-Chlorophenyldiazonium N-ethylphenylsulfamate. The diazo solution was added to a suspension of ethylphenylsulfamate. The reaction solution gradually colored, changing from pale yellow-orange to red. A small lustrous precipitate appeared. After the addition of a saturated solution of sodium acetate and cooling of the reaction mixture, a thick paste of crystals was formed and under a microscope, these appeared as plates. The precipitate was filtered off, washed with ice—water and pressed out on a porous plate, spread out as a very thin layer. The dehydrated precipitate had a browish yellow color with a gold luster; it dissolved almost completely in water to form a slightly yellow solution and coupled vigorously in neutral solution with H-acid and R-salt. During attempted recrystallizations from warm water and also on storage, even for a few hours, the substance decomposed.

Analysis for diazo component content: 0.5986 g of substance: 16.9 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_3N_3SCl$. Calculated: 17.6 ml of 0.1 N β-naphthol solution.

Sodium N-ethylphenylsulfamate and 4-nitro-2-chlorophenyldiazonium chloride. When the diazo solution was added to the suspension of ethylphenylsulfamate, the solution acquired an intense red-brown color. After several minutes, a fine, light brown precipitate formed. When filtered off and washed, the precipitate was insoluble in water. Under a microscope, it appeared as very fine, yellow crystals. The substance did not couple with an azo component in an aqueous solution. Consequently, it was not a diazo salt. It gave an intense color with α-naphthylamine in glacial acetic acid, which is characteristic of diazoamino compounds.

Sodium N-ethylphenylsulfamate and 2,5-dichlorophenyldiazonium chloride. The diazonium solution was added to a thick suspension of sodium ethylphenylsulfamate. The sulfamate precipitate gradually began to dissolve, forming a brown color. A brown precipitate formed, but not of the usual coarse, lustrous plates, characteristic of diazo salts, but of fine crystals, combined as flakes. The filtered and washed brown precipitate was insoluble in water. When heated with α-naphthylamine in glacial acetic acid, the substance formed a dye, which is characteristic of diazoamino compounds.

Synthesis of 2-anthraquinonyldiazonium sulfamate. 2-Aminoanthraquinone was diazotized by Schaarschmidt's method [12]. Anthraquinonyldiazonium chloride was recrystallized from warm water.

0.02 mole of sodium sulfamate was dissolved in a few milliliters of cold water and several drops of acetic acid added to it. With vigorous stirring, a solution prepared from 0.018 mole of 2-anthraquinonyldiazonium chloride was added. A slightly yellow precipitate formed almost immediately and after a few minutes, it filled the reaction vessel. The precipitate was filtered off and recrystallized from 10% acetic acid, acidified with several drops of hydrochloric acid and heated to 50-60°. A small amount of an insoluble residue was filtered off and the filtrate cooled in ice. Coarse golden yellow crystals precipitated immediately and under a microscope, they appeated as elongated plates. The precipitate was filtered off, washed with water and ether and dried in vacuum, pressed out on a porous plate.

Found %: diazo nitrogen 7.97. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated %: diazo nitrogen 8.02.

Analysis for diazo component content. A sample of the material was dissolved in 100 ml of 5% acetic acid, acidified with a few drops of hydrochloric acid. To the solution was added excess of 0.05 N solution of β-naphthol in alkali, adjusted to pH 7 by the addition of acetic acid. The solution being analyzed was brought to pH 7 with sodium bicarbonate, stirred for half-an-hour and the excess β-naphthol titrated with 0.05 N p-nitrophenyldiazonium solution.

0.2360 g of substance: 13.29 ml of 0.05 N β-naphthol solution. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated: 13.52 ml of 0.05 N β-naphthol.

Analysis for sulfamic acid content. A sample of the substance was dissolved as above. 10 ml of 5 N hydrochloric acid was added to the solution, which was titrated with 0.1 N nitrite solution.

0.6472 g of substance: 18.16 ml of 0.1 N nitrite solution. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated: 18.52 ml of 0.1 N nitrite solution.

SUMMARY

1. The reaction of diazo compounds with sulfamic, benzylsulfamic and N-ethylphenylsulfamic acids in an acid medium was investigated. Diazonium salts of these sulfamic acids were prepared.

2. It was shown that the diazonium salts of sulfamic acid and its alkyl- and aralkyl derivatives are colorless or only slightly colored. A strong color is only inherent in diazonium arylsulfamates.

3. It was established that the color of diazonium arylsulfamates did not depend on intermolecular reactions and depended little on the hydrogen bond, which may exist between the terminal nitrogen of the diazonium cation and the hydrogen on the imino group of the arylsulfamic acid.

4. It is proposed that the reason for color in diazonium arylsulfamates is a salt bond of peculiar character, which is capable of transmitting a conjugation effect between the electron acceptor diazonium cation and the electron donor arylsulfamate anion.

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Received April 6, 1957

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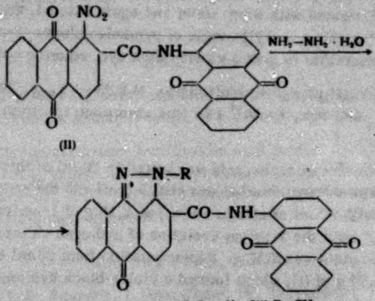
REACTION OF HYDRAZINE WITH NITRO COMPOUNDS OF THE ANTHRAQUINONE SERIES

II. SYNTHESIS OF VAT DYES – DERIVATIVES OF PYRAZOLEANTHRONECARBOXYLIC ACID

N. S. Dokunikhin and I. D. Pletneva

The previous report [1] describes the formation of pyrazoleanthrone derivatives by hydrazine treatment of nitro compounds of the anthraquinone series, among them 1-nitroanthraquinone-2-carboxylic acid and its phenylamide. A further development of this work was the application of the procedure found to the synthesis of more complex materials, possessing the properties of vat dyes. The patent literature [2, 3] describes the (1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid (I) as a yellow vat dye. We prepared this compound by treating the N-(1'-anthraquinonyl)-amide of 1-nitroanthraquinone-2-carboxylic acid (II) with hydrazine hydrate in pyridine and it was found to be the same as the product of acylating 1-aminoanthraquinone with the acid chloride of pyrazoleanthrone-2-carboxylic acid.

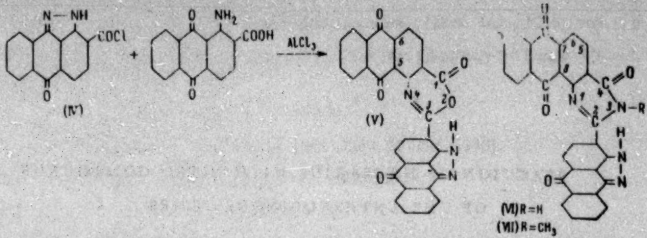


(II)

(I) $R = H$, (III) $R = CH_3$

Methylation of (I) gave an orange-yellow vat dye with structure (III).

New patents [4] describe the preparation of a series of vat dyes by the action of acid chlorides of substituted 2-anthraquinonecarboxylic acid in the presence of $FeCl_3$, $AlCl_3$ which, as a result of the simultaneous acylation and closing of the ring, gave derivatives of 5,6-phthaloyl-2,4,1-benzoxazine. When treated with ammonia and amines the latter readily exchanged the ring oxygen for nitrogen and were converted into the corresponding derivatives of 7,8-phthaloyl-3,4-dihydro-4-oxo-quinazoline [5]. On using the acid chloride of pyrazoleanthrone-2-carboxylic acid (IV) as an acylating agent one would expect a similar series of vat dyes with somewhat different shades. Treatment of 1-aminoanthraquinone-2-carboxylic acid with (IV) in the presence of $AlCl_3$ gave a compound which, according to analysis data, had structure (V) and when heated with aqueous ammonia exchanged oxygen for nitrogen to form substance (VI), that gave a vat dye coloring cellulose fibers dull yellow with a reddish tinge.



The corresponding compound (VII), prepared by using methylamine instead of ammonia, unexpectedly showed no affinity for cellulose fiber in contrast to similar derivatives of substituted anthraquinonecarboxylic acid that are vat dyes.

EXPERIMENTAL

3.85 g of the acid chloride of the 1-nitro-2-carboxylic acid of anthraquinone (m. p. 236-237°) was boiled in xylene with 2.32 g of 1-aminoanthraquinone (m. p. 250-251°) until the evolution of HCl ceased. The yield of the N-(1'-anthraquinonyl)-amide of the 1-nitro-2-carboxylic acid of anthraquinone (II) was 4.00 g.

Found %: N 5.72, 5.77. $C_{29}H_{14}O_7N_2$. Calculated %: N 5.58.

4.0 g of (II) and 10.0 g of hydrazine hydrate were boiled for 3 hrs in 40 ml of pyridine, diluted with water, filtered, washed free from pyridine and dried. The yield was 2.82 g of substance, which was dissolved in 25 ml of 90% H_2SO_4 and filtered through a glass filter and 6 ml of H_2O slowly added to the filtrate. The yellow rectangular prisms formed were filtered off, treated with warm water and again filtered, the acid washed off and the product dried to give 1.3 g of the N-(1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid (I), which reacted with an alkaline solution of hydrosulfite to give a violet-black dye, coloring cellulose fibers a bright lemon yellow.

Found %: N 8.98, 9.15. $C_{29}H_{15}O_4N_3$. Calculated %: N 8.95. λ_{max_1}320 mμ, $\epsilon \cdot 10^{-4}$ 2.26; λmin 400 mμ, $\epsilon \cdot 10^{-4}$ 1.35; λ_{max_2} 435 mμ, $\epsilon \cdot 10^{-4}$ 1.55 (the absorption spectrum of a water suspension of the dye was measured [6]).

2.64 g of pyrazoleanthrone-2-carboxylic acid was boiled in 20 ml of thionyl chloride (b. p. 75.5-76.5°) until a clear solution was formed. The thionyl chloride was distilled off and the residue, which consisted of yellow, hexagonal plates (IV), was treated with 30 ml of nitrobenzene and 2.23 g of 1-aminoanthraquinone (m. p. 250-251°). The mixture was heated at 150° until the vigorous evolution of hydrogen chloride ceased (about 36 hrs), filtered at 120°, washed and dried. The yield was 3.71 g. Reprecipitation from 33 ml of H_2SO_4 (90%) with 7.5 ml of H_2O (as described above) yielded 2.77 g of (I), which formed a violet-black hydrosulfite vat dye, coloring cellulose fibers lemon yellow.

Found %: N 8.83, 9.04. $C_{29}H_{15}O_4N_3$. Calculated %: N 8.95. λ_{max_1} 320 mμ, $\epsilon \cdot 10^{-4}$ 2.22; λ_{max_2} 400 mμ, $\epsilon \cdot 10^{-4}$ 1.38; λ_{max_3} 435 mμ, $\epsilon \cdot 10^{-4}$ 1.54.

2.35 g of dye (I) and 0.6 g of KOH were heated in 30 ml of $C_6H_5NO_2$ to 100°, a solution of 3.8 g methyl p-toluenesulfonate in 10 ml of $C_6H_5NO_2$ added over a period of 3 hrs, the mixture heated at 130° for 7.5 hrs and another 0.6 g of KOH added, followed by 3.8 g of methyl p-toluenesulfonate, added over a period of 3 hrs. The mixture was stirred at 130° for a further 6 hrs. The mixture was cooled and the precipitate filtered off and washed with methyl alcohol and water to yield 0.79 g of dye (III), which gave a black-violet alkaline hydrosulfite vat dye, coloring cellulose fibers orange-yellow.

λmin 309 mμ, $\epsilon \cdot 10^{-4}$ 0.43; λmax 460 mμ, $\epsilon \cdot 10^{-4}$ 0.60. Found %: N 8.40, 8.56. $C_{30}H_{17}O_4N_3$. Calculated %: N 8.69.

The acid chloride of pyrazoleanthrone-2-carboxylic acid, prepared from 9.24 g (0.035 mole) of pyrozoleanthrone-2-carboxylic acid (see above), was treated with 100 ml of dry nitrobenzene, 2.10 g of anhydrous $AlCl_3$

and 9.4 g (0.035 mole) of the 1-amino-2-carboxylic acid of anthraquinone. The reaction mixture was heated with stirring under an air condenser, fitted with a calcium chloride tube, up to 150° over a period of 3 hrs and then at 150° for 10-12 hrs until the vigorous evolution of hydrogen chloride ceased. Towards the end of the reaction, a sample under a microscope showed, instead of the original yellow hexagonals of the acid chloride and the crimson amorphous particles of 1-amino-2-carboxylic acid of anthraquinone, red-brown platelets. The mass was filtered hot and washed with 20 ml of nitrobenzene and 100 ml of benzene; we obtained 10.35 g of 5,6-phthaloyl-2,4,1-benzoxazine-3-(2'-pyrazoleanthronyl) (V).

Found %: C 72.33, 72.23; H 2.73, 2.77; N 8.15, 8.25. $C_{30}H_{23}O_5N_3$. Calculated %: C 72.73; H 2.64; N 8.48.

(V) gave a red-brown vat dye with hydrosulfite and alkali, which weakly colored cellulose fibers a pale yellow.

5 g of (V) was heated in a tube with 30 ml of 25% ammonia at 130° for 5 hrs. The brown precipitate formed was transferred to a filter and washed with water until there was no reaction with brilliant yellow paper. We obtained 4.72 g of (VI), which formed a black-green vat dye with alkaline hydrosulfite, coloring cellulose fibers yellow with a reddish tinge.

Found %: N 10.97, 10.95. $C_{30}H_{14}O_4N_4$. Calculated %: N 11.33. $\lambda_{\max_1}$ 310 mμ, $\epsilon \cdot 10^{-4}$ 4.09; $\lambda_{\max_2}$ 320 mμ, $\epsilon \cdot 10^{-4}$ 4.16; $\lambda_{\min}$ 400 mμ, $\epsilon \cdot 10^{-4}$ 1.85; $\lambda_{\max_3}$ 445 mμ, $\epsilon \cdot 10^{-4}$ 2.40.

2 g of (V) was heated in a tube with 40 ml of aqueous CH_3NH_2 solution (99 g of 1 liter) at 130° for 5 hrs. The precipitate was transferred to a filter and washed until there was no reaction to brilliant yellow paper. We obtained 1.88 g of 7,8-phthaloyl-3,4-dihydro-4-oxo-2-(2'-pyrazoleanthronyl)-quinazoline (VII), which dissolved when treated with hydrosulfite and NaOH solution. The leuco compound obtained in this way showed no affinity for cellulose fibers.

Found %: C 72.74, 72.73; H 2.99, 3.22; N 10.85, 10.83. $C_{31}H_{17}O_4N_4$. Calculated %: C 73.08; H 3.36; N 10.85.

SUMMARY

1. Treatment of the N-(1'-anthraquinonyl)-amide of the 1-nitro-2-carboxylic acid of anthraquinone with hydrazine hydrate gave the N-(1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid.

2. The acid chloride of pyrazoleanthrone-2-carboxylic acid reacted with 1-aminoanthraquinone-2-carboxylic acid in the presence of $AlCl_3$ to give 5,6-phthaloyl-2,4,1-benzoxazine-3-(2'-pyrazoleanthronyl), which gave 7,8-phthalolyl-3,4-dihydro-4-oxo-2-(2'-pyrazoleanthronyl)-quinazoline and 7,8-phthaloyl-3,4-dihydro-4-oxo-3-methyl-2-(2'-pyrazoleanthronyl)-quinazoline with ammonia and methylamine.

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Received March 16, 1957

Research Institute of Organic Intermediates and Dyes

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AZO DERIVATIVES OF CYANINE DYES

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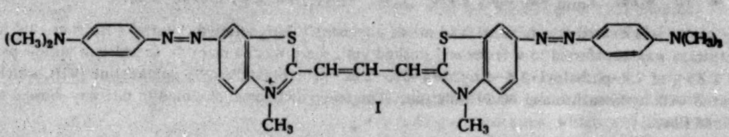
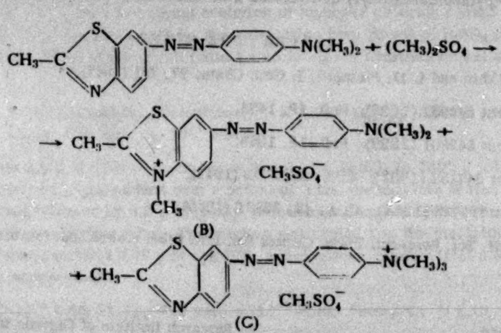
Cyanine dye analogs containing an azo group in the chromophore instead of a vinyl group have been described many times. They have been prepared, for example, by diazotizing 2-aminobenzthiazole derivatives and by coupling the diazo compounds obtained with active methyl or methylene groups of other nitrogen heterocycles [1]. However, typical cyanine dyes such as thiacarbocyanine (A) with arylazo groups as substituents in the benzene rings of the benzthiazole have not been prepared previously. Nevertheless, such dyes, which are simultaneously polymethine and azo dyes, are of definite value. They could explain whether an azo group together with a polymethine chain forms one common chromophore or whether the chromophores are, to a certain degree, disconnected here. It would also be valuable to determine the effect of the azo group on the sensitizing capacity of thiacyanines.



(A)

We synthesized a series of this type of dye, mainly thiacarbocyanines and styryls, starting with 2-methyl-5- and 2-methyl-6-arylazo derivatives of benzthiazole, whose preparation we recently described [2]. These bases were heated with dimethyl or diethyl sulfate and the quaternary salts obtained were condensed in the usual way to form cyanine dyes. One might expect that, in the case of dimethylaminophenylazo derivatives of 2-methylbenzthiazole, dimethyl sulfate molecules would be added not only to the nitrogen atom of the thiazole nucleus but also to the amine group to form two isomeric quaternary salts (B) and (C).



However, the quaternary salt we obtained was found to be capable of condensation to form styryls and carbocyanines and, consequently, was of structure (B) and not (C). In addition, if salt (C) was formed the effect of the

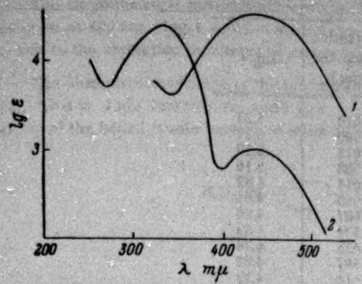


Fig. 1. Absorption spectra. 1) Methiodide of 2-methyl-6-p-dimethylaminophenylazobenzthiazole, 2) 2-methyl-6-phenylazobenzthiazole.

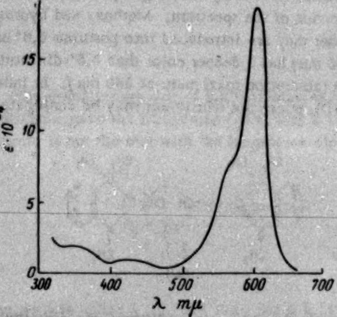


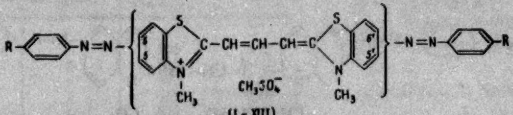
Fig. 2. Absorption spectrum of 3,3'-dimethyl-6,6'-di-(phenylazo)-thiacarboxyanine methyl sulfate.

amine group on light absorption would have been eliminated and the absorption curve of the salt would have approached the absorption curve of 2-methyl-6-phenylazobenzthiazole. Figure 1 shows that the substance we obtained differed a great deal in absorption from 2-methyl-6-phenylazobenzthiazole.

Due to the high molecular weight of the cyanine dyes prepared from the quaternary salts of 2-methylarylazo derivatives of benzthiazole, there were difficulties in purifying them. Even the methyl sulfates were difficultly soluble in the usual organic solvents. Therefore, the greater part of the dyes were purified not by crystallization but by boiling in alcohol and washing with hot alcohol and ether. As the analyses show, the preparations were purified sufficiently by this method.

The absorption curves of the dyes we prepared in alcohol solutions were determined on an SF-4 spectrophotometer. It was found that all the arylazothiacarbocyanines have one narrow and very intense absorption band, similar to the absorption band of unsubstituted thiacarbocyanine, but located in a much longer wavelength part of the spectrum. As an example, we give the absorption curve of one of the simplest dyes in this group – 6,6-diphenylazothiacarbocyanine (Fig. 2).

We see here one sharply expressed maximum at 610 mμ (ε 190500), consequently, both azo groups are conjugated with the polymethine chain, forming a common chromophore. Two weak absorption bands are also noticeable in the spectrum range from 320 to 480 mμ, with maxima at 350 mμ (ε 18,000) and 430 mμ (ε 7600). This section of the curve corresponds to the absorption of 2-methyl-6-phenylazobenzthiazole, which has the same two absorption bands – K-band with a maximum at 337 mμ and a weak R-band with a maximum at 435 mμ [2]. Thus, the absorption spectrum of a complex dye molecule has also partial chromophores which are characteristic of the corresponding aromatic azo compounds, and their bands are somewhat displaced towards the long wavelength section of the spectrum. The absorption curves of other symmetrical arylazocarbocyanines have a similar structure. Table 1 gives the absorption maxima and molecular extinctions of symmetrical arylazothiacarbocyanines (I-XIII) with the general formula



(I-XIII)

By comparing the absorption spectra of isomeric thiacarbocyanines, given in Table 1, which contain identical arylazo groups in positions 6,6' and 5,5', one may see that all 6,6' derivatives have absorption maxima that lie 30-38 mμ further towards the red end of the spectrum than those of 5,5' derivatives, with almost identical intensity of absorption. This interesting rule shows that the azo group is conjugated more readily with the polymethine chromophore through the nitrogen atom of the thiazole nucleus than through the sulfur atom. No such difference exists between the thiacarbocyanines containing simpler polar groups in positions 6,6' and 5,5'. Replace-

TABLE 1

Dye	R	Position of arylazo groups	Absorption maximum (in mμ)	log ε
(I)	H	6,6′	610	5.27
(II)	H	5,5′	580	5.27
(III)	OCH_3	6,6′	612	5.19
(IV)	OCH_3	5,5′	580	5.16
(V)	OH	6,6′	614	4.82
(VI)	OH	5,5′	580	4.84
(VII)	$OCOCH_3$	6,6′	607	4.80
(VIII)	$OCOCH_3$	5,5′	574	4.83
(IX *)	$N(CH_3)_2$	6,6′	635	4.78
(X **)	$N(CH_3)_2$	5,5′	597	4.82
(XI)	$NHCOCH_3$	6,6′	618	4.79
(XII)	SCH_3	6,6′	618	4.83
(XIII)	NO_2	6,6′	625	4.65

* Perchlorate.

** Iodide.

ment of the hydrogen atoms in positions 6,6' and 5,5' of a thiacarbocyanine by amino groups also displaces the absorption maximum by 40 mμ towards the long wavelength section of the spectrum. Methoxy and hydroxy groups also affect thiacarbocyanine absorption in the same way, whether they are introduced into positions 6,6' or 5,5'. Only 6,6'-dinitrothiacarbocyanine (absorption maximum at 585 mμ) has a deeper color than 5,5'-dinitrothiacarbocyanine (absorption maxi mum at 560 mμ). In indocarbocyanines (D), where the substituent may be conjugated with the chain only through a nitrogen atom, the dimethylamino groups in positions 5,5' displace the absorption maximum 60 mμ towards the long wavelength section of the spectrum and in positions 6,6' – only by 23 mμ [3].

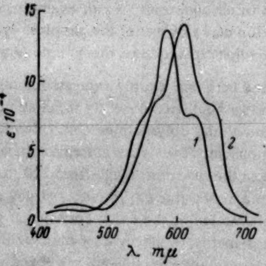
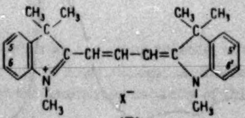


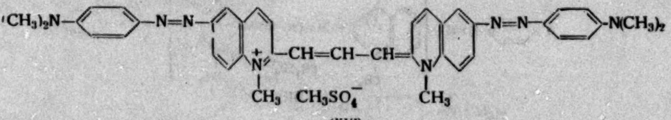
Fig. 3. Absorption spectra. 1) Biscyanine (XIX), 2) biscyanine (XX).



(D)

Among the symmetrical bisarylazothiacarbocyanines we prepared mesoethyl substituted dyes (I) (XIV, λ_{max} 605 mμ, log ε 4.82) and dyes (VI) (XV, λ_{max} 570 mμ, log ε 4.90). As usual, their absorption maxima are somewhat displaced towards the short wavelength section of the spectrum.

One quinocarbocyanine (XVI) was also synthesized.

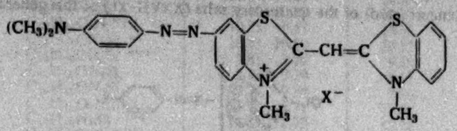


(XVI)

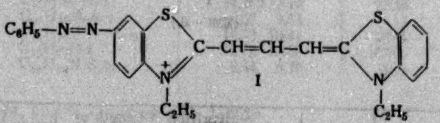
Its color is much deeper and more intense (λ_{max} 670 mμ, log ε 5.28) than that of the thiacarbocyanines (IX) corresponding to it and like the majority of quinocyanines it has a second shorter wavelength absorption maximum (λ_{max} 625 mμ, log ε 4.98).

The unsymmetrical monomethinecyanine (XVII) we synthesized has, in addition to the main absorption maximum at 490 mμ (log ε 4.85), a second, less intense maximum at 420 mμ (log ε 4.44), which probably corresponds to the absorption maximum of monomethinecyanine (422 mμ).

The absorption maximum of the unsymmetrical thiacarbocyanine (XVIII) we prepared lies at 580 mμ (log ε 4.90). This is 4 mμ less than the additive value; consequently, the phenylazo group quite strongly lowers the basicity of the benzthiazole nucleus to which it is connected.

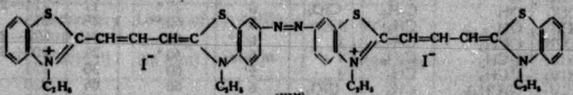


(XVII)



(XVIII)

The diquaternary salt of 2,2'-dimethyl-6,6'-azobenzthiazole and the ethiodide of 2-ω-acetanilidovinylbenzthiazole gave the biscyanine (XIX) with a very unusual absorption curve (Fig. 3, curve 1). The most intense maximum is not the one with the longest wavelength (λ_{max} 620 mμ, log ε 4.89), but the one next to it towards shorter wavelengths (λ_{max} 588 mμ, log ε 5.14). Apparently, the long wavelength band corresponds to the absorption of the conjugation chain, which passes through the whole dye molecule and the next, more intense band corresponds to the absorption of that part of the molecule which includes thiacarbocyanine with one azo group (see dye XVIII). A similar absorption band (λ_{1max} 640-665 mμ, log ϵ_1 4.94, λ_{2}max 610 mμ, log ϵ_2 5.15, $\lambda_3$max 570 mμ, log ϵ_3 4.93) is found in the case of the biscyanine (XX), which was prepared from the same azobenzthiazole and the ethiodide of 2-ω-acetanilidovinylquinoline (Fig. 3, curve 2).

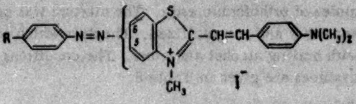


(XIX)

TABLE 2

Dye	R	Position of azo group	Absorption maximum (in mμ)	log ε
(XXI)	H	6	560	4.81
(XXII)	OCH_3	6	560	4.77
(XXIII *)	$OCOCH_3$	6	565	4.82
(XXIV)	SCH_3	6	565	4.86
(XXV **)	$N(CH_3)_2$	6	573	4.79
(XXVI)	$N(CH_3)_2$	5	553	4.78

The different effect on light absorption of arylazo groups in positions 5 and 6 of the benzthiazole nucleus was observed not only in the appropriate carbocyanines but also in styryl dyes. Table 2 gives the absorption maxima and the molecular extinctions of styryls (XXI-XXVI) with the general formula as seen below



(XXI - XXVI)

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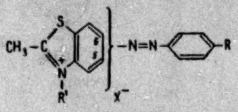
* Perchlorate.

** Methyl sulfate.

EXPERIMENTAL

Quaternary salts. All the quaternary salts, used as starting materials in the synthesis of dyes, were prepared by heating 2-methyl-5- or 2-methyl-6-arylazo derivatives of benzthiazole, which we described previously [2], on a water bath with 1.5 mole of dimethyl sulfate or diethyl sulfate in benzene solution. For purification and analysis, the methyl and ethyl sulfates obtained were boiled with active charcoal in aqueous solution and precipitated with potassium iodide or sodium perchlorate in the form of the iodides or perchlorates, which were recrystallized from water. The dyes were prepared from unpurified alkyl sulfates. In Table 3 are given the conditions of preparation and melting points (uncorrected) of the quaternary salts (XXVII-XL) of the general formula



(XXVII - XL)

TABLE 3

Quaternary salts	R	R′	X	Position of azo group	Length of heating (in min)	Yield (in %)	Melting point (decomp.)
(XXVII)	H	CH_3	I	6	60	47	226—227°
(XXVIII)	H	C_2H_5	I	6	30 *	29	232—233
(XXIX)	H	CH_3	I	5	60	61	198
(XXX)	OH	C_2H_5	ClO_4	6	25 *	17	214—215
(XXXI)	OH	CH_3	I	5	60 **	45	215
(XXXII)	OCH_3	CH_3	I	6	60	34	220—221
(XXXIII)	OCH_3	C_2H_5	I	6	40 *	29	205—206
(XXXIV)	OCH_3	CH_3	I	5	60	30	224
(XXXV)	$N(CH_3)_2$	CH_3	ClO_4	6	60	66	220
(XXXVI)	$N(CH_3)_2$	CH_3	I	5	60	39	163
(XXXVII)	NO_2	CH_3	ClO_4	6	60	33	240—241
(XXXVIII)	$NHCOCH_3$	CH_3	I	6	60	33	231—233
(XXXIX)	SCH_3	CH_3	I	6	60	54	218—219
(XL)	Cl	CH_3	ClO_4	6	60	60	238

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* At 120° without solvent.

** At 100° in nitrobenzene.

The methiodide of 6-p-dimethylaminophenylazoquinaldine (XLI) was prepared similarly. The yield was 43% and the m. p. 218° (with decomp.).

The diethiodide of 2,2'-dimethyl-6,6'-azobenzthiazole (XLII) was prepared by heating the base with 3 moles of dimethyl sulfate for 40 min at 120°. The iodide, prepared by adding potassium iodide to the aqueous solution, was recrystallized twice from water. The yield was 90% of orange needles with m. p. 236-237° (with decomp.). The results of analyzing the salts listed are given in Table 4.

Dyes. The symmetrical carbocyanines were prepared by the usual method. 0.2-0.4 g of the quaternary salt (for the most part unrecrystallized methyl sulfate) in 3-5 ml of dry pyridine was boiled under reflux with 4 moles of orthoformic ester. The mixture was cooled and the precipitated dye filtered off, washed with alcohol and ether and recrystallized. The dyes which were difficultly soluble in alcohol, were simply purified by washing with boiling alcohol and ether. The conditions of preparation, yields and melting points of the symmetrical carbocyanines are given in Table 5.

TABLE 4

Quaternary salts	Empirical formula	N (%)	
		found	calc.
(XXVII)	$C_{15}H_{14}N_3SI$ *	10.54, 10.53	10.63
(XXVIII)	$C_{16}H_{16}N_3SI$	10.17, 10.21	10.27
(XXIX)	$C_{15}H_{14}N_3SI$	10.60, 10.57	10.63
(XXX)	$C_{16}H_{16}O_5N_3SCl$	10.35, 10.47	10.58
(XXXI)	$C_{15}H_{14}ON_3SI$ **	10.33, 10.30	10.22
(XXXII)	$C_{16}H_{16}ON_3SI$ ***	9.81, 9.76	9.88
(XXXIII)	$C_{17}H_{18}ON_3SI$	9.22, 9.29	9.56
(XXXIV)	$C_{16}H_{16}ON_3SI$	9.74, 9.70	9.88
(XXXV)	$C_{17}H_{16}O_4N_4SCl$	13.72, 13.77	13.66
(XXXVI)	$C_{17}H_{19}N_4SI$ ****	12.89, 12.73	12.78
(XXXVII)	$C_{15}H_{13}O_6N_4SCl$	13.71, 13.89	13.53
(XXXVIII)	$C_{17}H_{17}ON_4SI$	12.26, 12.14	12.39
(XXXIX)	$C_{16}H_{16}N_3S_2I$	9.39, 9.34	9.52
(XL)	$C_{15}H_{13}O_4N_3SCl_2$	10.32, 10.41	10.45
(XLI)	$C_{19}H_{21}N_4I$	12.72, 12.82	12.96
(XLII)	$C_{20}H_{22}N_4S_2I_2$	8.54, 8.78	8.80

* Found %: I 32.16, 32.18. Calculated %: I 32.15.

** Found %: I 30.33, 30.34. Calculated %: I 30.94.

*** Found %: I 29.85, 29.69. Calculated %: I 29.88.

**** Found %: I 29.05, 29.19. Calculated %: I 28.99.

TABLE 5

Dyes (see Table 1)	Quaternary salts (see Table 3)	Length of boiling (in min)	Crystallization solvent	Yield (in %)	Melting point (decomp.)	External appearance of dye
(I)	(XXVII *)	20	Alcohol	44	265—266°	Blue needles
(II)	(XXIX *)	25	Alcohol	64	283	Violet needles with a metallic luster
(III)	(XXXII *)	20	CH_3OH	58	240	Prisms with a metallic luster
(IV)	(XXXIV *)	20	CH_3OH	34	243	Violet powder
(V)	(XXX)	20	CH_3OH	37	217—218	Dark blue powder
(VI)	(XXXI *)	25	—	34	251	Violet powder
(VII)	(XXX)	20 ***	CH_3OH	42	237—238	Dark blue powder
(VIII)	(XXXI *)	25 ***	—	28	289—290	Violet powder
(IX)	(XXXV)	25	—	59	249—250	Green needles
(X)	(XXXVI)	20	—	23	253—254	Blue crystals
(XI)	(XXXVIII *)	25 ****	—	46	254	Green needles
(XII)	(XXXIX *)	30	—	50	259—260	Green needles
(XIII)	(XXXVII *)	40	Nitrobenzene	65	267—268	Dark powder
(XIV)	(XXVIII)	20 **	Alcohol	42	222	Blue needles
(XV)	(XXXI *)	20 **	Alcohol	15	226	Violet powder
(XVI)	(XLII)	20	—	42	246	Green needles

* Methyl sulfate.

** Orthopropionic ester was used instead of orthoformic.

*** The solvent was acetic anhydride.

**** The solvent was a mixture of pyridine and acetic anhydride.

The unsymmetrical carbocyanine (XVIII) was prepared by boiling a mixture of 0.1 g of 2-methyl-6-phenylazobenzthiazole ethiodide, 0.1 g of 2-ω-acetanilidovinylbenzthiazole ethiodide, 0.05 g of anhydrous sodium acetate and 2 ml of acetic anhydride for 20 min. When the substance had been crystallized from alcohol, the yield was 0.07 g (50%) and the m. p. 237-238° (with decomp.).

TABLE 6

Dyes (see Table 2)	Quaternary salts (see Table 3)	Crystallization solvent	Yield (in %)	Melting point (decomp.)	External appearance of dye
(XXI)	(XXVII)	—	77	243—244°	Green needles
(XXII)	(XXXII *)	—	42	225—226	Green prisms
(XXIII)	(XXX **)	—	37	268—269	Green prisms
(XXIV)	(XXXIX *)	CH_3OH	54	234—235	Green prisms
(XXV)	(XXXV)	Alcohol	48	206	Dark blue powder
(XXVI)	(XXXVI *)	CH_3OH	40	216	Violet powder

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* Iodide.

** Perchlorate.

For the synthesis of the monomethinecyanine (XVII), we boiled a mixture of 0.32 g of 2-methyl-6-p-diaminophenylazobenzthiazole methylmethyl sulfate, 0.16 g of anhydrous sodium acetate and 0.25 g of 2-methylmercaptobenzthiazole methyl methyl sulfate in 6 ml of anhydrous alcohol for 1 hr. For purification, the dye was chromatographed in a chloroform solution on aluminum oxide. After extracting with boiling alcohol, we obtained 0.11 g (25%) of dark red needles with m. p. 264° (with decomp.).

The bisthiacarbocyanine (XIX) was synthesized from 0.3 g of 2,2'-dimethyl-6,6'-azobenzthiazole diethiodide and 0.41 g of 2-ω-acetanilidovinylbenzthiazole ethiodide, which were heated in acetic anhydride with anhydrous sodium acetate. When recrystallized from alcohol, it formed a dark blue powder. The yield was 0.21 g (44%) and the m. p. 150-152° (with decomp.).

Similarly, from the same diquaternary salt and 2-ω-acetanilidovinylquinoline ethiodide we obtained a 39% yield of the bisthiaquinocarbocyanine (XX) as a dark blue powder with m. p. 228° (with decomp.).

TABLE 7

Dyes	Empirical formula	N (%)	
		found	calculated
(I)	$C_{32}H_{28}O_4N_6S_3$	12.65, 12.95	12.80
(II)	$C_{32}H_{28}O_4N_6S_3$	12.68, 12.79	12.80
(III)	$C_{34}H_{32}O_6N_6S_3$	11.69, 11.67	11.73
(IV)	$C_{34}H_{32}O_6N_6S_3$	11.52, 11 64	11.73
(V)	$C_{32}H_{28}O_6N_6S_3$	12.15, 12.12	12.21
(VI)	$C_{32}H_{28}O_6N_6S_3$	12.37, 12.30	12.21
(VII)	$C_{36}H_{32}O_8N_6S_3$	10.74, 10.69	10.88
(VIII)	$C_{36}H_{32}O_8N_6S_3$	10.71, 10.77	10.88
(IX)	$C_{35}H_{35}O_4N_8S_2Cl$	15.08, 15.16	15.34
(X)	$C_{35}H_{35}N_8S_2I$	14.50, 14.61	14.78
(XI)	$C_{36}H_{34}O_6N_8S_3$	14.28, 14.34	14.54
(XII)	$C_{34}H_{32}O_4N_6S_5$	11.16, 11.14	11.23
(XIII)	$C_{32}H_{26}O_8N_8S_3$	14.72, 14.61	15.01
(XIV)	$C_{35}H_{33}N_6S_2I$	11.60, 11.49	11.54
(XV)	$C_{34}H_{32}O_6N_6S_3$	11.69, 11.70	11.73
(XVI)	$C_{40}H_{42}O_4N_8S$	15.43, 15.36	15.34
(XVII)	$C_{26}H_{27}O_4N_5S_3$	12.39, 12.28	12.30
(XVIII)	$C_{27}H_{25}N_4S_2I$	9.34, 9.30	9.40
(XIX)	$C_{42}H_{40}N_6S_4I_2$	8.21, 8.25	8.32
(XX ***)	$C_{46}H_{44}N_6S_2I_2$	8.34, 8.37	8.42
(XXI)	$C_{24}H_{23}N_4SI$	10.53, 10.57	10.64
(XXII)	$C_{25}H_{25}ON_4SI$	10.22, 10.29	10.07
(XXIII)	$C_{26}H_{25}O_6N_4SCl$	9.86, 10.01	10.07
(XXIV)	$C_{25}H_{25}N_4S_2I$	9.64, 9.57	9.79
(XXV)	$C_{27}H_{31}O_4N_5S_2$	12.48, 12.57	12.66
(XXVI)	$C_{26}H_{28}N_5SI$	12.22, 12.28	12.30

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* Found %: I 25.26, 25.07. Calculated %: I 25.45.

All the styryl dyes, listed in Table 2, were synthesized from the appropriate quaternary salts by boiling them in acetic anhydride with an equivalent amount of p-dimethylaminobenzaldehyde for 20 min. The precipitate of dye was crystallized from alcohol or washed with boiling alcohol and ether. The preparation conditions of various styryl dyes and some of their properties are given in Table 6.

Table 7 gives the analysis results for all the dyes described in this work.

SUMMARY

The quaternary salts of 2-methyl-5- and 2-methyl-6-arylazobenzthiazoles gave a series of symmetrical and unsymmetrical thiacyanines and styryls, containing arylazo groups as substituents in the benzene rings. It was found that the absorption spectra of these dyes had one intense absorption band. Consequently, the azo group and polymethine chain form one common chromophore. The absorption bands of 6-arylazo derivatives of thiacyanines are displaced considerably towards the red end of the spectrum in comparison with those of the 5-arylazo derivatives.

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[2] A. I. Kiprianov and I. P. Fedorova, Ukrain. Chem. J. 21, 76 (1955); 23, 59 (1957).

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Received January 8, 1957 Kiev State University

THE REACTION OF HYDRAZINE WITH CARBON DISULFIDE

EXPERIMENTS ON THE SYNTHESIS OF DIISOTHIOCYANOGEN

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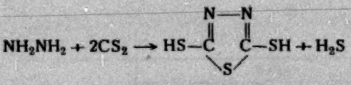
Previously, one of us had shown that under certain conditions alkylene diisothiocyanates may be prepared using a modified Calus method [1]. It seemed interesting to use a similar method for preparing the simplest representative of this series of compounds – diisothiocyanogen SCN–NCS, which was previously unknown. The scheme for such a synthesis may be represented by the following equations

$$NH_2NH_2 + 2CS_2 + 2NaOH \longrightarrow \underset{(I)}{(NHCSSNa)_2} \qquad (1)$$

$$(NHCSSNa)_2 + 2ClCOOC_2H_5 \longrightarrow \underset{(II)}{(NHCSSCOOC_2H_5)_2} \qquad (2)$$

$$(NHCSSCO_2C_2H_5)_2 \xrightarrow{\text{pyrolysis}} \underset{(III)}{(NCS)_2} + 2COS + 2C_2H_5OH \qquad (3)$$

Hydrazine reacted with carbon disulfide (excess) by Busch's method, to form 1,5-dithiol-1,3,4-thiadiazole and not hydrazinebisdithiocarbonic acid.



Hydrazinebisdithiocarbonic acid derivatives were prepared by the reaction of hydrazine with potassium thiocyanate (diamide) [3] or with diethyl trithiocarbonate (diethyl ester) [4].

$$HSCN + NH_2NH_2 \longrightarrow (NHCSNH_2)_2$$

$$SC(SC_2H_5)_2 + NH_2NH_2 \longrightarrow (NHCS_2C_2H_5)_2 + C_2H_5SH$$

Hydrazinebisdithiocarbonic acid itself or its salts had not been prepared previously.

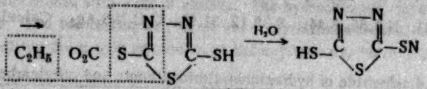
It was found that the sodium salt of this acid (I) was readily prepared by reacting hydrazine (1 mole) with carbon disulfide (2 moles) in the presence of sodium hydroxide (2 moles) in an aqueous medium and precipitating the salt with acetone from the solution thus formed (equation 1). The disodium salt thus obtained rapidly decomposed when heated and stored in air: however, it could be kept for weeks at a low temperature. Addition of silver or lead nitrate to the aqueous salt solution precipitated the silver or lead salts of the acid, which were difficultly soluble in water. The former was relatively stable and could be analyzed.

Thus, the first stage of the proposed synthesis was achieved without any special difficulties. The next stage also presented no difficulties – the preparation of the mixed dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids (II) (equation 2). Disodium salt (I) reacted with ethyl chloroformate in an aqueous medium to give a poor yield of (II), apparently because of the instability of the salt in an aqueous solution; this compound was prepared in better yield in a benzene or ether medium. In contrast to the salt of hydrazinebisdithiocarbonic acid, its dianhydride derivative was stable and could be recrystallized.

The last stage of the synthesis planned was carried out by pyrolyzing dianhydride (II) at 140-150° in vacuum. However, instead of the expected diisothiocyanogen (III) (or its polymer) we obtained an oily substance with b. p. 143-145° (1 mm) which did not contain an isothiocyanate group. The presence of an ethoxyl group in this product and its hydrolysis with 15% hydrochloric acid to a crystalline compound with m. p. 167° and other properties, which correspond to Busch's 2,5-dithiol-1,3,4-thiadiazole [2] indicated that the substance obtained had the structure of 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate (IV). Its formation, apparently, occurred by the scheme

$$(NHCSSCO_2C_2H_5)_2 \rightarrow [S{=}C{=}N{-}NH{-}CSSCO_2C_2H_5 \rightleftarrows$$

$$\rightleftarrows S{=}C{=}N{-}N{=}C(SH)SCO_2C_2H_5]$$



(IV)

The ease of such a cyclization with the formation of 1,3,4-thiadiazole derivatives was noted earlier using samples of the diamide and diethyl ester of hydrazinebisdithiocarbonic acid [3, 4]. Pyrolysis of dianhydride (II) under more drastic conditions at 250° also did not produce diisothiocyanogen. The main reaction product in this case, besides the tarry residue, was ethyl thiocyanate. The formation of ethyl thiocyanate may be explained by the thermal decomposition of the ester of the thiadiazole derivative (IV), which formed, apparently, as an intermediate product in this reaction (shown in the scheme by a dotted line). This observation and the hypothetical scheme of ethyl thiocyanate formation indicate that thiocyanates could possibly be obtained in other cases of the thermal decomposition of compounds containing $RO_2C{-}SCN$ groups.

The thermal decomposition of methyl and ethyl esters of thiocyanocarbonic acid, which we investigated in connection with the above, confirmed this hypothesis; in both cases the corresponding alkyl thiocyanates were obtained in yields of 50-60% of the theoretical.

$$ROCOSCN \rightarrow CO_2 + RSCN$$

In order to avoid cyclization which occurred when dianhydride (II) was heated during the preparation of diisothiocyanogen, we decided to synthesize the analogous, less stable compound – the dianhydride of hydrazinebisdithiocarbonic and chlorocarbonic acids (V), during whose decomposition we might also expect the formation of diisothiocyanogen.

$$(NHCS_2Na)_2 + 2COCl_2 \xrightarrow{-2NaCl} \underset{(V)}{(NHCS_2COCl)_2} \xrightarrow[-COS]{-2HCl} (NCS)_2$$

Actually, material (V), hygroscopic yellow crystals, formed by reacting phosgene with the disodium salt of hydrazinedithiocarbonic acid, was unstable at room temperature, but in the absence of moisture could be kept at low temperatures (from −70° to −80°). Its composition was as expected; however, no diisothiocyanogen was formed when it decomposed at room temperature and under other conditions (in the presence of bases to bind the HCl). Thus, the two methods planned for synthesizing diisothiocyanogen did not give positive results.

Several attempts have been made to prepare materials analogous to diisothiocyanogen. Thus, at various times, Nef, Tiele and Staudinger tried to synthesize diisocyanogen OCN−NCO [6], diisonitrile CN−NC [5] and cyanocarbylamine NC−NC [7] but were unsuccessful. It remains to be clarified to what degree all these failures, including ours, are due to the use of unsuitable methods for preparing this type of compound. It is possible that the materials named are not formed due to their extreme instability, which precludes the existence of these compounds, in contrast to such known pseudo-halogens as dicyanogen and dithiocyanogen.

EXPERIMENTAL

1. The reaction of hydrazine with carbon disulfide. Preparation of salts of hydrazinebisdithiocarbonic acid $(NHCS_2Me)_2$. With vigorous stirring, a solution of 6 g of hydrazine hydrate in 10 ml of water was added dropwise to a mixture of 16 g of freshly distilled carbon disulfide and 16 ml of 50% aqueous sodium hydroxide. The tem-

perature of the reaction mixture rose to 45° and then fell to room temperature. The orange-yellow solution obtained was kept for a further 30 min at 40°, then cooled in ice and salt and treated with cold acetone until the oil (lower layer) was completely precipitated. Seed crystals of the disodium salt of hydrazinebisdithiocarbonic acid were added to the cooled mass and then the lower layer was triturated until friable crystals formed and these were separated, washed with acetone and dried in vacuum. (The seed was prepared by triturating 0.5 ml of liquid from the lower layer with several portions of acetone with cooling in a carbon dioxide mixture.) We obtained 23 g of colorless crystals of the disodium salt.

0.5 g of the crystals were dissolved in 5 ml of cold water and mixed with a concentrated solution of $AgNO_3$. 0.7 g of the disilver salt was precipitated.

Found %: C 5.87, 5.61; N 6.58, 6.44; S 32.12, 31.91. $C_2H_2N_2S_4Ag_2$. Calculated %: C 6.03; N 7.03; S 32.2.

2. Preparation of the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids (II). With stirring, 16 g of ethyl chloroformate was added dropwise to a mixture of 15 g of disodium hydrazinebisdithiocarbonate and 70 ml of dry ether at such a rate that there was a slow rise in the temperature of the reaction mixture to 40°. When all the ethyl chloroformate had been added, the flask was kept at 50° for 2 hrs. The precipitate of sodium chloride formed was separated and the filtrate evaporated in vacuum. We obtained 12.5 g of crystals, which were freed from the oil covering them by dissolution in chloroform and reprecipitation with ether (4-fold dilution), while cooled with carbon dioxide. Subsequent recrystallization from alcohol yielded colorless needles with m. p. 87°.

Found %: C 30.31, 30.24; H 3.58, 3.52; N 8.84, 8.75; S 38.66; OC_2H_5 26.96, 26.85. M 313 (in benzene). $C_8H_{12}O_4N_2S_4$. Calculated %: C 29.2; H 3.67; N 8.5; S 39.6; OC_2H_5 27.4. M 327.

3. Thermal decomposition of the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids. Preparation of 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate (IV). 3 g of the dianhydride (II) was heated at 140-150° for 30 min. The oil formed was vacuum distilled. We obtained 2 g of a colorless oil with an ester smell and b. p. 143-145° (2 mm), d^{20}_{20} 1.299.

Found %: OC_2H_5 19.93, 19.34. M 212.5 (in benzene). $C_5H_6O_2N_2S_3$. Calculated %: OC_2H_5 20.3. M 222.

0.5 g of the substance was heated at 100° for 5 hrs in an ampule with 5 ml of 15% hydrochloric acid. The oil crystallized on cooling. The crystals were pressed out on a porous plate and recrystallized from ether with carbon dioxide cooling. We obtained needles with m. p. 167° and other properties corresponding to 2,5-dithiol-1,3,4-thiadiazole [2].

4. Pyrolysis of dithiolthiadiazole ethylcarbonate (IV). 8 g of the ethylcarbonate with b. p. 143-145° (2 mm) was placed in a distillation flask and heated with a burner for 30 min. In the receiver we collected 3.2 g of a colorless liquid, distilling in the range 100-160°. The residue in the flask was carbonized. A second distillation yielded a fraction with b. p. 140-143° (1.5 g), d^{20}_{20} 1.005, $n^{20}D$ 1.4670, with the characteristic smell and properties of ethyl thiocyanate (see below for its constants).

Found %: C 40.87; H 5.64; N 15.15. M 83.5. C_3H_5NS. Calculated %: C 41.4; H 5.75; N 16.1. M 87.

5. Pyrolysis of ethyl thiocyanocarbonate. Preparation of ethyl thiocyanate. 5 g of ethyl thiocyanocarbonate with b. p. 83-85° (30 mm), prepared by Dixon and Teylor's method [8], was boiled under reflux for 2 hrs. The substance darkened and carbon dioxide was evolved. The tarry residue was distilled on a semimicrocolumn (6 theoretical plates). A fraction with b. p. 141-143° (2.0 g) had d^{20}_{20} 1.007, $n^{20}D$ 1.4675 and was identified as ethyl thiocyanate. The yield of ethyl thiocyanate was 60%. (According to literature data: b. p. 143.6°, $d^{22.9}_4$ 1.0071, $n^{22.9}D$ 1.4684 [9]).

Found %: N 15.73. M 84.3. C_3H_5NS. Calculated %: N 16.1. M 87.0.

6. Pyrolysis of methyl thiocyanocarbonate. Preparation of methyl thiocyanate. 5 g of methyl thiocyanocarbonate with b. p. 30° (12 mm), prepared by Dixon and Teylor's method [8], was treated as described in Expt. 5. We isolated 1.7 g of a colorless liquid with b. p. 132-133°, d^{20}_{20} 1.0730, $n^{20}D$ 1.4725, which was methyl thiocyanate. The yield was 55% of the theoretical. (According to literature data: b. p. 131°, d^{15}_4 1.0765, $n^{15}D$ 1.4745 [9]).

Found %: N 18.87. M 70.5. C_2H_3NS. Calculated %: N 19.2. M 73.0.

7. Reaction of disodium hydrazinebisdithiocarbonate with phosgene. A cooled solution of 21 g of phosgene in 100 ml of chloroform was added to a suspension of 10 g of the disodium salt in 50 ml of chloroform, which was stirred at a temperature of −5 to −6°. After 10 hrs, the sodium chloride was separated and the solvent evaporated in vacuum (all operations with the exclusion of moisture). We isolated 5.5 g of yellow hygroscopic crystals with the chracteristic smell of phosgene. The substance was unstable and decomposed in air forming a coarse orange powder with decomp. p. 100° and which was insoluble in water and the usual solvents.

Found %: C 15.95; N 10.71; Cl 23.51; S 39.98. M 297 (in benzene). $C_4H_2O_2N_2S_4Cl_2$. Calculated %: C 15.5; N 9.1; Cl 23.0; S 41.5. M 309.

1.2 g of the substance was mixed with 3 ml of aniline. The hydrochloride and excess aniline were washed out with 5% hydrochloric acid. The insoluble part (0.6 g) was recrystallized from alcohol. We obtained prisms with m. p. 237°. A mixed melting point with symmetrical diphenylurea was not depressed.

SUMMARY

1. Reaction of hydrazine with carbon disulfide in an aqueous-alkaline medium gave the disodium salt of hydrazinebisdithiocarbonic acid. This salt reacted with chlorocarbonic ester and phosgene to form the corresponding dianhydrides $(NHCS_2CO_2C_2H_5)_2$ and $(NHCS_2COCl)_2$.

2. When heated to 150° the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids was converted into 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate, which at 250° split to form ethyl thiocyanate. This did not give diisothiocyanogen. Diisothiocyanogen was also not obtained by decomposition of the dianhydride of hydrazinebisdithiocarbonic and chlorocarbonic acids.

3. It was shown that alkylthiocyanocarbonic esters decompose when heated, to form alkyl thiocyanates.

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Received January 25, 1957

A METHOD OF OBTAINING FLUORINE DERIVATIVES OF SILICON, TIN, AND SULFUR

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Among metalloorganic compounds methods are known for replacing alkoxyl groups on the metal with chlorine by the action of inorganic or organic acid chlorides. The possible analogous replacement of alkoxyl groups with fluorine by a reaction with organic acid fluorides has not yet been specifically studied. It appeared interesting to us to study this reaction in alkoxyl derivatives of silicon, tin, and sulfur.

As we have shown, the fluorides of carboxylic acids, and especially the easily obtained acetyl fluoride, react with alkoxyl derivatives of these elements, transforming them into the corresponding fluorides by the general scheme

$$R_mEl(OR')_{n-m} + CH_3COF \longrightarrow R_mEl(OR')_{n-m-1}F + CH_3COOR'.$$

This reaction goes easily when the central atom bound to the alkoxyl group is an electropositive element. Thus, alkoxy tin derivatives in the reaction with acetyl fluoride exchange their alkoxyl groups for fluorine even in the cold. In the case of compounds of silicon and sulfur the exchange occurs with heating. In all cases the fluorine compound is formed in good yield. When the ratio of the reagents is changed (in the case of polyalkoxy compounds) it is possible to replace not only one, but also a larger number of alkoxyl groups. Thus, for example, from diethyl diethoxytin it is possible to obtain mono- and difluorides. From tetraethoxytin with excess acetyl fluoride it is easy to form tin tetrafluoride which was first synthesized by Ruff [1] with great experimental difficulty. The reaction of acetyl fluoride with alkoxysilanes was studied with the example of tetrabutoxysilane. In this case, heating to 180° formed tributoxyfluorosilane in 60-70% yield. It should be noted that before our study, Peppard, Brown, and Johnson [2] investigated the reaction of tetraethoxysilane with benzoyl fluoride; however, they did not find an exchange of alkoxy groups for fluorine.

Polyfluorosilanes are apparently easier to obtain by the Grignard reaction from silicon tetrafluoride, as we found earlier in the synthesis of ethylsilane fluorides [3].

$$SiF_4 \xrightarrow{RMgX} RSiF_3 \xrightarrow{RMgX} R_2SiF_2$$

The reaction of acetyl fluoride with alkoxysulfur compounds was studied with dimethyl sulfate. In this case formation of methyl fluorosulfonate occurred with 60% yield when the vapors of acetyl fluoride were passed into boiling dimethyl sulfate. It follows from these results that the action of carboxylic acid fluorides on alkoxy derivatives of different elements is evidently a general method for the synthesis of the corresponding fluorine derivatives. Since the starting alkoxyl derivatives of these elements and the acid fluorides are usually easy to obtain, this method has general preparative interest.

EXPERIMENTAL

1. Obtaining diethyl ethoxytin fluoride. The vapor of acetyl fluoride (1.2 g) was passed into a solution of 5 g of diethyl ethoxytin in 30 ml of absolute ether at room temperature (mole ratio 1:1). The mixture grew warm and at the end of the experiment colorless crystals of difluoride precipitated. These were filtered (0.8 g) and the filtrate was evaporated. The residue was a low melting, white, crystalline mass (3.5 g) which was pressed between sheets of filter paper to the consistency of a powder which can be poured. Diethyl ethoxytin fluoride melts at 90-91°.

The substance is soluble in ether and benzene. It changes with keeping: the melting point rises and becomes unsharp (105-112°). The molecular weight determination of diethyl ethoxytin fluoride (in benzene) shows that it associates.

Found %: F 8.08, 7.60; OC_2H_5 19.17. M 453, 462. $(C_6H_{15}OFSn)_2$. Calculated %: F 7.92; OC_2H_5 18.7. M 481.4.

2. Obtaining diethyltin difluoride. 2 g of diethyl diethoxytin was dissolved in 10 ml absolute ether and the solution treated with vapors of acetyl fluoride. The precipitated crystals were filtered and washed with ether. Diethyltin difluoride was crystallized from anhydrous alcohol. Yield 1.4 g (85%).

Found %: C 22.05, 21.62; H 5.12, 4.34; F 16.55, 16.42. $C_4H_{10}F_2Sn$. Calculated %: C 22.38; H 4.65; F 17.70.

3. Obtaining tin tetrafluoride. 10 g tetraethoxytin was dissolved in 40 ml of benzene. The cooled solution was treated with acetyl fluoride (4 moles with 10% excess). After the solution was heated to boiling, the precipitate of tin tetrafluoride was filtered, washed with benzene, and dried. Yield, 4 g. The tin tetrafluoride thus obtained was an almost colorless, finely crystalline substance which deliquesces in air.

4. Obtaining tributoxyfluorosilane. 10 g (1 mole) of tetra-(n-butoxy)-silane and 2.3 g (1 mole) of acetyl fluoride were heated in a sealed tube 8 hrs at 150° and then 4 hrs at 180°, after which the product was fractionated. Tri-(n-butoxy)-fluorosilane, boiling 133-134° (32 mm) or 125-125.5° (30 mm), d^{20}_{20} 0.9383, was obtained in the amount of 3.8 g.

Found %: F 7.19, 7.30. $C_{12}H_{27}OFSi$. Calculated %: F 7.14.

5. Obtaining ethyltrifluorosilane. Silicon tetrafluoride was passed with cooling (−60°) and energetic stirring into 500 ml of absolute ether. An ether solution of 1 mole of ethylmagnesium bromide in 600 ml of ether was added to the reaction mixture through a tube which led to the bottom of the flask, and slowly, dropwise over 2 hrs, so that the temperature in the reaction mixture did not rise above −60°, after which the addition of silicon tetrafluoride was continued for another 15 min. Then the contents of the flask along with the acetic acid which had condensed in it were distilled. The fraction with boiling point to +10° was redistilled repeatedly. We obtained 45 g of ethyltrifluorosilane boiling at −4-2°. The yield was about 40% (based on magnesium).

Found %: F 49.52. M 113.4. $C_2H_5F_3Si$. Calculated %: F 49.91. M 114.1.

6. Obtaining diethyldifluorosilane. The synthesis was carried out in a manner analogous to that of Expt. 5. Saturation with gaseous SiF_4 took place at 10-15°. The introduction of 1 mole of ethylmagnesium chloride was carried out dropwise over 45-50 min. After the ether was distilled off in a column with 10 theoretical plates the residue was fractionated. We obtained 10 g of diethyldifluorosilane with boiling point 61.5-62°.

Found %: F 30.65. M 124.0 (in benzene). $C_4H_{10}F_2Si$. Calculated %: F 30.60. M 124.1.

7. Obtaining methyl fluorosulfonate. The vapors of acetyl fluoride (7 g) were bubbled into 12.5 g of freshly distilled dimethyl sulfate at the boiling point. Reaction was energetic. In the receiver, connected to a reflux condenser, we collected about 4 ml of unreacted acetyl fluoride which was returned to the reaction mixture. By repeated redistillations we obtained 3 g of methyl acetate, boiling 57-58°, 3.5 g of a mixture of methyl acetate with methyl fluorosulfonate boiling 75-80°, and 4.5 g of methyl fluorosulfonate boiling 92°, d^{20}_{20} 1.3998. 2 g of dimethyl sulfate and about 1 g of acetyl fluoride did not enter into reaction. The yield of methyl fluorosulfonate was 50-60% based on reacting dimethyl sulfate.

SUMMARY

We have studied the reaction of acetyl fluoride with alkoxy derivatives of Sn, Si and S; we have found that in this reaction there occurs replacement of alkoxy groups by fluorine with formation of the corresponding fluoroorganic compounds.

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Received February 22, 1957

THE TAUTOMERISM OF 9-AMINOACRIDINE

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Spectrographic study in the ultraviolet of 2- and 4-amino- [1], 2- and 4-hydroxy- [2], and 2- and 4-methylpyridine [3] has shown that tautomerism of these substances, according to absorption spectra, does not occur. The literature on the spectrum study of 9-aminoacridine [4-7, 11, 12] is contradictory. In the present paper we consider the absorption spectrum in the ultraviolet of 9-aminoacridine and 10-methyl-9-iminoacridine.

The synthesis of these substances was carried out according to the literature data [8, 9]. 9-Aminoacridine after recrystallization from acetone formed light yellow crystals with m. p. 236° (236-237° [10]). 10-Methyl-9-iminoacridine after recrystallization from absolute ether appeared as light orange needles with m. p. 134-136° (134-136° [9], 134° [7]).

We repeated in part the studies described in the literature of 9-aminoacridine in ethanol, dioxane and weak solutions of hydrochloric acid and sodium alcoholate, and also ran studies in comparatively concentrated solutions of hydrochloric, sulfuric, and nitric acids. 10-Methyl-9-iminoacridine also was studied spectroscopically in ether, hexane, and dioxane with addition of small amounts of water. In all the solvents, the studies were carried out at 10^{-3} to 10^{-5} molar concentrations. 10-Methyl-9-iminoacridine was studied in dioxane from 10^{-2} to 10^{-5} molar, and in hexane, because of the great insolubility, from 10^{-4} to 10^{-5} molar solutions.

The absorption spectrum of 9-aminoacridine in organic solvents is characterized by two very intense absorption bands which lie between λ 4400-3200 and 2800-2400 A (Fig. 1, curves 1 and 2). Comparison of the absorption spectrum of acridine in ethanol and 9-aminoacridine in ethanol and dioxane (Fig. 1, curves 1, 2, and 3) shows that they are similar, except that the absorption curve for 9-aminoacridine differs from the curve for acridine by a shift toward the visible. Under the influence of the amino group the long wave "benzene" maximum of acridine is shifted by 500 A, and the short wave maximum by 100 A; the intensities of these bands remain almost unchanged. In general, the spectrum of 9-aminoacridine in organic solvents can be considered as a complex "benzeneaminopyridine" absorption spectrum, in which the "pyridine" and "p-aminopyridine" bands are not clearly apparent. However, the "p-aminopyridine" band with a maximum oriented at about λ 2600 A is seen in the spectra of its derivatives, 2-methoxy-9-aminoacridine (Fig. 1, curve 4), and the "pyridine" band with an approximate maximum at λ 3125 A (one of the bands in the fine structure of pyridine) was detected by Acheson [7] on the curve of 9-aminoacridine in methanol.

9-Dimethylaminoacridine, studied as a standard of the tautomeric amino form [7], has in its absorption spectrum a satisfactory similarity to 9-aminoacridine (Fig. 1, curve 5) and differs from the latter only in the fine structure of the long wave "benzene" band. Such a fine structure of the "benzene" band is also found in its derivative, 2-methoxy-9-aminoacridine (Fig. 1, curve 4).

In the standard solutions of hydrochloric acid in ratios 1 : 0.1, 1 : 1, and 1 : 100 moles of HCl (Fig. 1, curves 6-8) the absorption spectrum of 9-aminoacridine shows a fine structure in its long wave "benzene" band with λmax 4235, 4000, and 3800 A, and a fine structure in the "pyridine" bands with λmax 3250 and 3100 A, but a "p-aminopyridine" band with a maximum about λ 2600 A, as in the neutral solutions, is not clearly seen. Evidently, it is covered by the more intense "benzene" band of 9-aminoacridine with the same maximum at about λ 2600 A.

The fine structures of the "benzene" and "pyridine" bands seen in the absorption spectra of acid solutions of 9-aminoacridine when the concentration of hydrochloric acid changes in wide limits from 0.1 to 5 M (Fig. 1, curves 7-9, cf. curve 11) indicate that 9-aminoacridine forms a salt [4] like 4-aminoacridine [1] with just 1 equiv. of acid.

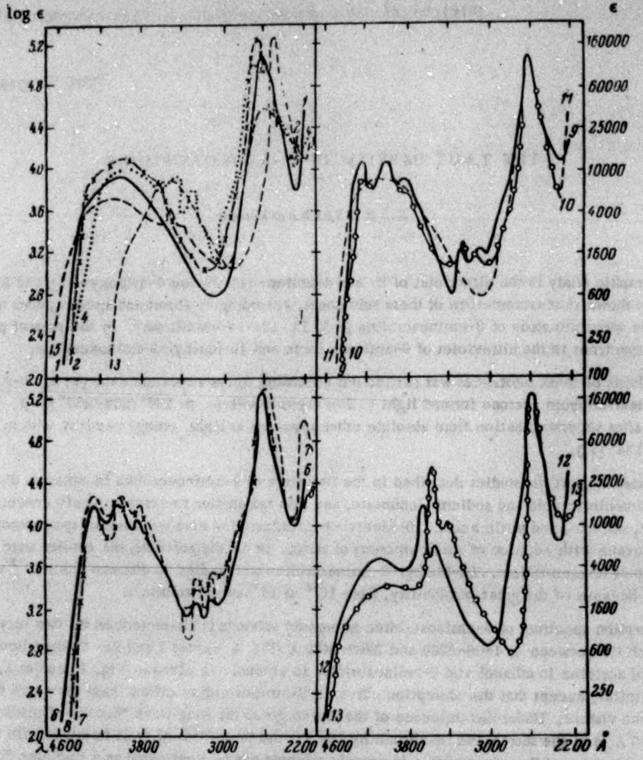


Fig. 1. Absorption spectra. 1) 9-Aminoacridine in ethanol, 2) 9-aminoacridine in dioxane, 3) acridine in ethanol, 4) 2-methoxy-9-aminoacridine in ether, 5) 9-dimethylaminoacridine in methanol [7], 6) 9-aminoacridine in ethanol solution of HCl (1 : 0.1), 7) 9-aminoacridine in ethanol solution of HCl (1 : 1), 8) 9-aminoacridine in ethanol solution of HCl (1 : 100), 9) 9-aminoacridine in 5 molar ethanol solution of HCl, 10) 9-aminoacridine in 20% H_2SO_4 (after dilution of a water solution in 17.5 M H_2SO_4), 11) 9-aminoacridine in ethanol, 12) 9-aminoacridine in concentrated (17.5 M) H_2SO_4, 13) acridine in 17.5 M H_2SO_4.

The absorption spectrum of 9-aminoacridine in concentrated sulfuric acid approximates to the structure of unsubstituted acridine (Fig. 1, curves 12 and 13), in the same acid. This can be explained, in spite of the literature data [13], by the formation of a salt also on the amino group. In order to determine whether sulfonation of 9-aminoacridine by concentrated sulfuric acid occurs, we diluted the solution to 20% sulfuric acid. The absorption spectrum in 20% sulfuric acid (Fig. 1, curve 10) agreed with the curve for absorption in the standard 5 M solution of hydrochloric acid (Fig. 1, curve 9). This confirms that in concentrated sulfuric acid there is only salt formation.

A study of the absorption spectrum of 10-methyl-9-iminoacridine in anhydrous hexane, ether, and dioxane (Fig. 2, curves 1-3) showed that it had nothing in common with the spectra of 9-aminoacridine and 9-dimethyl-

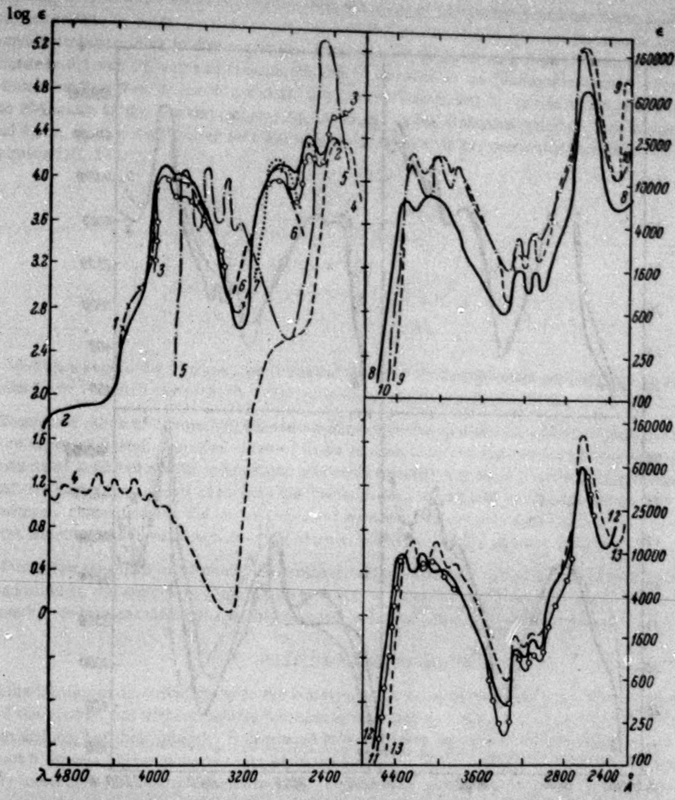


Fig. 2. Absorption spectra. 1) 10-Methyl-9-iminoacridine in ether, 2) 10-methyl-9-iminoacridine in dioxane, 3) 10-methyl-9-iminoacridine in hexane, 4) p-benzoquinone [14] in hexane, 5) anthracene in hexane, 6) dihydroacridine in ethanol [15], 7) diphenyl amine in ethanol [16], 8) 10-methyl-9-iminoacridine in water, 9) 9-aminoacridine in alcohol solution of HCl (1 : 1), 10) 9-aminoacridine hydrochloride in ethanol, 11) 10-methyl-9-iminoacridine in ethanol solution of HCl (1 : 100), 12) 10-methyl-9-iminoacridine in 5 M ethanol solution of HCl, 13) 9-aminoacridine in 5 M ethanol solution of HCl.

aminoacridine in the same solvents. Comparison of the absorption spectrum of 10-methyl-9-iminoacridine and p-benzoquinone [14] (Fig. 2, curves 1 and 4) in hexane showed their similarity. The absorption maxima of the three bands occurred almost at the same wavelength and only two of them differed in intensity. It is interesting that one of the three absorption bands at a maximum of λ 2900 A and ε 12,000 is also characteristic for dihydroacridine [15] and diphenyl amine [16]. When we compare the absorption spectrum of 10-methyl-9-iminoacridine with the absorption spectrum of anthracene (Fig. 2, curves 1 and 5) we can see that the bands with maxima at λ 3950 A and ε 12,000, λ 3800 A, ε 9000, and λ 2650 A, ε 20,000 are "benzene" bands. Hence the absorption spectrum of 10-methyl-9-iminoacridine must be regarded as complex: "benzene" bands are superimposed on the "quinone" spectrum.

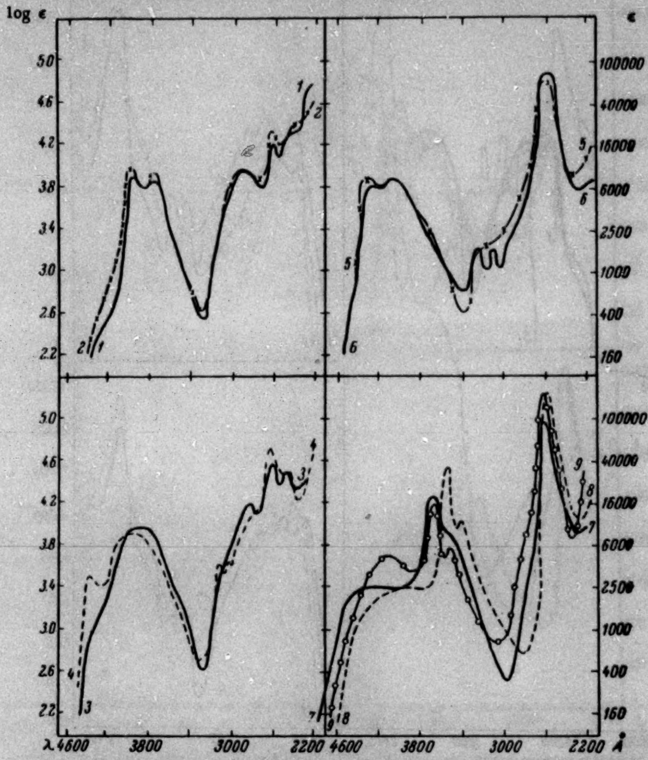
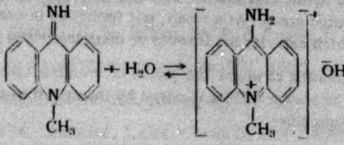


Fig. 3. Absorption spectra. 1) 10-Methyl-9-iminoacridine in dioxane—water solution (0.1% water), 2) 10-methyl-9-iminoacridine in dioxane—water solution (2% water), 3) 10-methyl-9-iminoacridine in dioxane—water solution (10% water), 4) 10-methyl-9-iminoacridine in dioxane—water solution (water 20%), 5) 10-methyl-9-iminoacridine in dioxane—water solution (50% water), 6) 10-methyl-9-iminoacridine in water, 7) 10-methyl-9-iminoacridine in 17.5 M H_2SO_4, 8) acridine in 17.5 M H_2SO_4, 9) 9-aminoacridine in 17.5 M H_2SO_4.

Under the influence of such polar solvents as water and also in acid solutions there is a strong change in the absorption spectrum of 10-methyl-9-iminoacridine; its character is like that of 9-aminoacridine in ethanolic hydrochloric acid (Fig. 2, curves 8-12). This similarity occurs because of salt formation both for 10-methyl-9-iminoacridine and for 9-aminoacridine which form acridine ions with the same structure.

The absence of "quinone" bands in the spectrum of 9-aminoacridine dissolved in organic solvents or in acids, and the actually observed "pyridine" bands in its absorption spectrum confirm the correctness of the conclusion concerning the amine structure of 9-aminoacridine.

Considering that in water solution the absorption spectrum of 10-methyl-9-iminoacridine is identical with that of 9-aminoacridine in acids, we tried to prepare equilibrium mixtures of the two tautomeric forms by dissolving 10-methyl-9-iminoacridine in dioxane–water solutions with different quantities of water in the dioxane. When we added between 0.1 and 2% water to dioxane, no change was seen in the "benzene-quinone" spectrum of 10-methyl-9-iminoacridine (Fig. 3, curves 1 and 2). Equilibrium was shifted to the side of the amino form at contents of 2 to 30% water in the dioxane (scheme A). A change in the absorption spectrum then occurred (Fig. 3, curves 3 and 4). A similar equilibrium reaction with water in dioxane has previously been observed for N-methyl-α-pyridoneimine [18, 19].



(A)

With 40–50% water in the dioxane, the "quinone" bands of 10-methyl-9-iminoacridine were not observed (Fig. 3, curves 5 and 6) which indicates the practically complete transformation of the imino to the amino form.

The absorption curve of 10-methyl-9-iminoacridine dissolved in dioxane–water solutions was compared with the absorption curve of 9-aminoacridine obtained under conditions of catalytic action on it of ethanol solutions of small amounts of acid and alkali; comparison was made immediately after preparing the solutions of 9-aminoacridine, and two days later. In all cases only the "benzene-aminopyridine" bands were observed in the 9-aminoacridine spectrum, characterizing the amino form, and no similarity was seen with the curves of 10-methyl-9-iminoacridine which would have shown an equilibrium of both forms of the assumed tautomers.

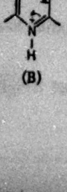
The absorption spectrum of 10-methyl-9-iminoacridine in concentrated sulfuric acid hardly differs from that of 9-aminoacridine in the same acid (Fig. 3, curves 7 and 9). Such a resemblance in spectra indicates the formation in 10-methyl-9-iminoacridine of a doubly charged cation like that of 9-aminoacridine.

DISCUSSION OF RESULTS

The introduction of an amino group in the acridine ring in position 9 causes a marked shift in the "benzene" bands toward the visible, but without notable increase in their intensity compared to acridine, while the "pyridine" bands are not shifted, but their intensity is decreased in nonionizing solvents by about 6 times, and in ionizing solvents by about 3 times. This may be because when the benzene and aminopyridine rings are condensed in 9-aminoacridine they interact, as in 4-aminoquinoline [17]. Two types of interaction are seen: 1) interaction of the condensed benzene and pyridine rings; "benzene" and "pyridine" bands are seen in the spectrum; 2) interaction of the amino group with the ring and the ring nitrogen. The weak participation of the amino group in union with the π-electrons of the pyridine ring in the study of 9-aminoacridine in nonionizing solvents can be explained by association of the molecules [13, 20, 21].

The effect of such ionizing solvents as an ethanol solution of hydrogen chloride even at ratios of 9-aminoacridine and HCl of 1 : 0.1 (9-aminoacridine is insoluble in water) causes separation of the associated molecules and the formation of 9-aminoacridine ions in whose spectra the "pyridine" bands with fine structure are clearly visible.

In the ion there is a redistribution of electron density from the amino group to the positively charged nitrogen (scheme B). A combination occurs between the amino groups, the π-electrons of the pyridine ring, and the electron-attracting ring nitrogen which is similar to that found in 4-aminopyridine or 4-aminoquinoline [1, 17].



(B)

Simultaneously with the appearance in the spectra of ethanol solutions of 9-aminoacridine of "pyridine" bands with fine structure, there should occur "p-aminopyridine" bands corresponding to the combination of groups. However, such "p-aminopyridine" bands with maxima at about λ 2600 A were not observed only because they were covered by the more intense short wave "benzene" bands with maxima at the same wavelength.

Profiting by the fact that when OH, OCH_3 or NH_2 groups are introduced into the benzene ring of 9-aminoacridine the "benzene" bands undergo a bathychromic shift, we succeeded in showing clearly in 2-methoxy-9-aminoacridine that "p-aminopyridine" band absorption was present.

When salts of 9-aminoacridine are formed, its "benzene aminopyridine" absorption spectrum is almost unchanged, which indicates that 9-aminoacridine is a tautomeric compound. Actually, in an ethanol solution of hydrochloric acid the absorption spectrum of 10-methyl-9-iminoacridine is identical with the spectrum of salts of 9-aminoacridine formed on the ring nitrogen.

This similarity of the spectra of 9-aminoacridine and 10-methyl-9-iminoacridine in acids even with their different structures can be explained by the fact that in the first, the salt-forming center is the ring nitrogen and in the second, the nitrogen of the imino group. As a result, salt formation in each case will give an ion of 9-aminoacridine with the same structure, which explains the identity of their absorption spectra in acid média.

These data do not solve the question of where the proton of 9-aminoacridine is actually found: on the ring nitrogen, or on the amino group. The answer will be obtained by investigation of 10-methyl-9-iminoacridine in anhydrous dioxane, hexane, or absolute ether.

In the spectrum of 10-methyl-9-iminoacridine in anhdrous dioxane, for example, there are bands which correspond to quinone or quinone imine. Close similarity also exists with dihydroacridine or diphenyl amine with band maximum at λ 2900 A.

In the spectrum of 9-aminoacridine in the same solvents we observed "pyridine" bands and did not find "quinone imine" or "diphenylamine" absorption bands. On the basis of this difference we assumed an amine structure for 9-aminoacridine and so we should reject the hypothetical tautomeric imino form.

The data of our spectrographic study of the amine structure of 9-aminoacridine agree with the measurements of dipole moment. The observed dipole moment of 9-aminoacridine is 4.13 D [22], which considerably exceeds the dipole moment calculated on its amino group, 3.28 D. The excess of the dipole moment of 0.85 D above the calculated value confirms the correctness of our spectrographic data, that between the ring nitrogen, the π-electrons of the pyridine ring, and the amino group of 9-aminoacridine there is a combination. In the absence of such a combination of the amino group with the ring nitrogen through the π-electron system of the pyridine ring, the dipole moment calculated on the imino form of 9-aminoacridine should be 1.65 D, which does not agree with the experimental value.

The double reactive ability of 9-aminoacridine can be explained in accord with the views of A. N. Nesmeianov [23, 24] by the course of reaction with a transferred reaction center.

SUMMARY

1. We have studied the effect of solvents and acids on the absorption spectrum of 9-aminoacridine and 10-methyl-9-iminoacridine.

2. We have shown that the "benzene-aminopyridine" absorption spectrum of 9-aminoacridine is almost unchanged when salts are formed on the ring nitrogen.

3. Salt formation by 9-aminoacridine in concentrated sulfuric acid is characterized by the formation of a doubly charged 9-aminoacridine cation.

4. We have shown that the absorption spectra of 9-aminoacridine and 10-methyl-9-iminoacridine in anhydrous dioxane are different, but are similar in solutions of hydrogen chloride and concentrated sulfuric acid.

5. We have shown that 9-aminoacridine in ethanol solutions of hydrochloric acid forms salts by binding the proton on the ring nitrogen, and in 10-methyl-9-iminoacridine, on the nitrogen outside the ring.

6. We have established the absence of tautomerism in 9-aminoacridine by the ultraviolet absorption spectrum.

In conclusion, I express deep thanks to V. I. BliznIukov, under whose direction this investigation has been carried out.

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Received November 29, 1956

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THE SYNTHESIS OF 5,6,7-TRIMETHYLISOALLOXAZINES

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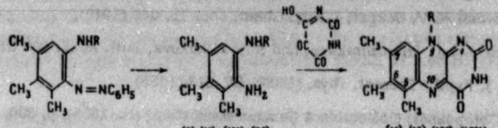
We have earlier shown [1] that a methyl group in the ortho-position to the azo group in 3,4,5-trimethylphenyl-2-phenylazo-1-D-glucamines, which are starting substances for the synthesis of isoalloxazines, causes stereochemical difficulties in reaction and a strong shift in ultraviolet absorption bands. It was interesting to trace this effect on the spectral characteristics of isoalloxazine compounds themselves when a methyl group was in positions 5, 6, and 7, reflecting the structure of riboflavin (positions 6 and 7) and also the structure of one of the stronger antivitamins, isoriboflavin [2] (positions 5 and 6). Since the spacial isomerism of the pentose side chain of 3,4-dimethylphenyl-1-D-glucamine affects its reactivity [3], we also tested the effect of such isomerism in 3, 4,5-trimethylphenyl-2-amino-1-D-glucamines (I-IV). For a solution of these problems we prepared 5,6,7-trimethylisoalloxazines (V-VIII) with tetrahydroxyalkyl substituents in position 9 which corresponded to the configurations of the hydroxy groups of all four possible pentose groups: D-ribose, D-arabinose, D-xylose, and D-lyxose. The corresponding 3,4,5-trimethyl-2-phenylazo-1-D-glucamines were transformed by catalytic hydrogenation into 3,4,5-trimethyl-o-phenylenediamino compounds (I-IV) which were condensed with alloxane into isoalloxazines (V-VIII); condensation was carried out at 50° in the presence of boric acid as a catalyst.



(I),(II),(III),(IV)

(V),(VI),(VII),(VIII)

R = pentose residues: d-ribose (I and V), d-arabinose (II and VI), d-xylose (III and VII), and d-lyxose (IV and VIII).

Isoriboflavin [4] was obtained from 3,4-dimethylphenyl-2-phenylazo-1-D-ribose amine which was reduced to 3,4-dimethylphenyl-2-amino-1-D-ribose amine; this diamine was condensed with alloxane.

The absorption spectra of riboflavin, isoriboflavin, and the new 5,6,7-trimethylisoalloxazines (V-VIII) are characterized by the data given in Table 1 and shown in Fig. 1.

TABLE 1

Substance	Position of CH_3 groups	Relative ultraviolet fluorescence	Absorption maximum							
			1		2		3		4	
			λ mμ	$\varepsilon \cdot 10^4$	λ mμ	$\varepsilon \cdot 10^4$	λ mμ	$\varepsilon \cdot 10^4$	λ mμ	$\varepsilon \cdot 10^4$
Riboflavin	6 & 7	100	223	2.86	268	3.15	372	1.06	445	1.19
Isoriboflavin	5 & 6	21	—	—	268	3.38	382	1.06	448	0.67
Trimethyliso-alloxazine derivatives (V-VIII)	5,6 & 7	20–23	223	2.27	268	3.21	394	1.44	446	0.88

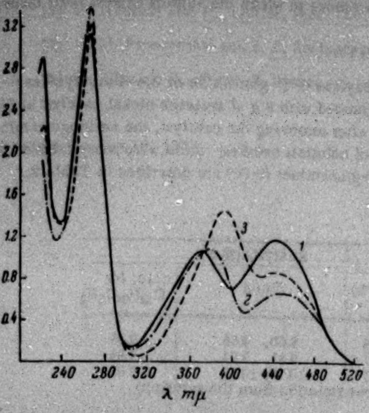


Fig. 1. Ultraviolet absorption spectra (in water). 1) 6,7-Dimethyl-9-(1'-D-ribityl)-isoalloxazine (riboflavin); 2) 5,6-dimethyl-9-(1'-D-ribityl)-isoalloxazine (isoriboflavin); 3) 5,6,7-trimethyl-9-(1'-D-ribityl)-isoalloxazine.

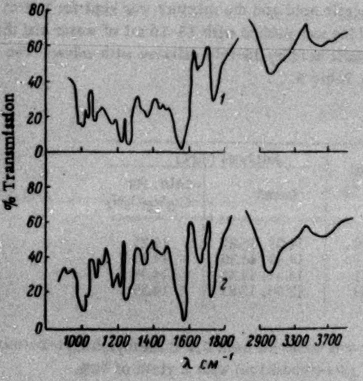


Fig. 3. Infrared absorption spectra (in CCl_4). 1) 5,6,7-Trimethyl-9-(1'-D-ribityl)-isoalloxazine; 2) 6,7-dimethyl-9-(1'-D-ribityl)-isoalloxazine (riboflavin) (d = 500 μ).

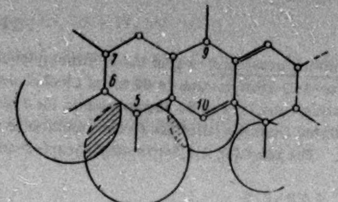


Fig. 2.

The introduction of a methyl group in the position "peri" to the hetero-nitrogen atom causes a strong decrease in intensity of absorption up to 60-70% in the visible. There then occurs a shift in the 3rd ultraviolet maximum of 10 mμ for isoalloxazines with methyl groups in positions 5 and 6, and of 22 mμ for derivatives with methyl groups in positions 5, 6, and 7 of the isoalloxazine ring.

No effect of configuration of hydroxyls of the pentoses substituted in the 3,4,5-trimethylphenyl-2-amino-D-glycamines was observed in the condensations with alloxane.

The shift in ultraviolet absorption maxima and the decreased intensity of absorption in the visible part of the spectrum for isoalloxazines with a large substiuent in the position "peri" to the hetero-nitrogen must be regarded as involving spatial difficulties, forcing this nitrogen atom out of the plane of the ring and at the same time breaking the coplanar structure of the system of conjugated double bonds $-\underset{10}{N}=\underset{|}{C}-\overset{|}{C}=\underset{1}{N}-$ into which enters the azomethine chromophoric group $-N=C<$ (cf. Fig. 2).

Flavins have a typical ability to fluoresce, and some of them glow intensely in ultraviolet light. It is known that introduction of a methyl group in the position "peri" to the hetero-nitrogen atom (position 5) causes a sharp decrease in intensity of fluorescence; this confirms the idea that just the system of conjugated double bonds, coplanar with the plane of the molecule, gives the flavin its power to fluoresce.

For 5,6-dimethyl-9-(1-D-ribityl)-isoalloxazine (riboflavin) and 5,6,7-trimethyl-9-(1-D-ribityl)-isoalloxazine (V), using the method of infrared absorption, we obtained the oscillation spectra at frequencies 800-1800 cm^{-1} and 2700-4000 cm^{-1} (Fig. 3). The introduction of an additional methyl groups in the isoalloxazine ring does not make much change in the spectra and in the characteristic frequencies of the groups C=C, C=N, and C=O. The absorption maxima in the oscillation frequencies of OH, CH, and NH are the same in these two spectra, and the absorption curves of the latter groups overlap and cannot be fully resolved.

The infrared absorption spectra were taken by L. V. Luk'ianova to whom the authors express their thanks.

EXPERIMENTAL

Aminoglucamines. 3 g of 3,4,5-trimethylphenyl-2-phenylazo-1-D-glucamine or 3,4-dimethylphenyl-2-phenylazo-1-D-ribitylamine in 60 ml of alcohol were hydrogenated with 3 g of skeleton nickel catalyst at 85-100° in a rotating autoclave at 60 atmos pressure for 3 hrs. Then, after removing the catalyst, the aminoglucamines were isolated from the colorless alcohol solution in the form of colorless needles; these were recrystallized from alcohol. The resulting 3,4,5-trimethylphenyl-2-amino-1-D-glucamines (I-IV) are described in Table 2.

TABLE 2

Substance	Substituent R	Melting point	Yield (in %)	Analysis (% N) found	Analysis (% N) calc. for $C_{14}H_{24}O_4N_2$
(I)	D-Ribityl	137—138°	58	9.60, 9.66	9.85
(II)	D-Arabityl	141—143	77	9.81, 9.94	9.85
(III)	D-Xylityl	137—138	71	10.19, 10.13	9.85
(IV)	D-Lyxityl	(Used without isolation from the solution)			

3,4,-Dimethylphenyl-2-amino-1-D-ribitylamine was obtained as colorless needles, melting at 138-140°, yield 37%.

Found %: N 10.06, 9.93. $C_{13}H_{22}O_4N_2$. Calculated %: N 10.36.

Isoalloxazines. To a solution of 2 g alloxane in 30 ml boiling glacial acetic acid was added a boiling solution of 4 g of boric acid in 30 ml of glacial acetic acid. The partly crystallized boric-alloxane complex was treated at 50° with 2 g of aminoglucamine in 30 ml of glacial acetic acid and the mixture was kept for 1 hr at 50°. Then the solvent was distilled off in a vacuum, the dry residue was washed with 10-15 ml of water and the flavin was reprecipitated from 8-10 ml of concentrated hydrochloric acid by 15-fold dilution with water. The resulting 5,6,7-trimethylisoalloxazines (V-VIII) are described in Table 3.

TABLE 3

Substance	Substituent R	Melting point	Yield (in %)	Analysis (%N) found	Analysis (%N) calc. for $C_{18}H_{22}O_6N_4$
(V)	D-Ribityl . . .	269° (decomp.)	50	14.03, 13.89	14.35
(VI)	D-Arabityl . . .	279 (decomp.)	75	14.32, 14.20	14.35
(VII)	D-Xylityl . . .	282 (decomp.)	51	14.24, 14.46	14.35
(VIII)	D-Lyxityl . . .	278 (decomp.)	33	13.90, 13.85	14.35

Isoriboflavin, 5,6-dimethyl-9-(1-D-ribityl)-isoalloxazine was obtained from 3,4-dimethylphenyl-2-amino-1-D-ribitylamine in the form of yellow needles melting at 264° (decomposition) with a yield of 70%.

Found %: N 14.87, 14.84. $C_{17}H_{20}O_6N_4$. Calculated %: N 14.88.

SUMMARY

1. We have shown that the fluorescence of isoalloxazines is due to the conjugated system $-\mathrm{N}{=}\underset{|}{\mathrm{C}}-\overset{|}{\mathrm{C}}{=}\mathrm{N}-$ and its intensity depends on the coplanarity of this system with the plane of the molecule.

2. We have obtained 8 new compounds of which 4 are new flavins.

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Received January 10, 1957

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ESTERS OF AMINOPHENYLSULFONAMIDOPHOSPHORIC ACID

A. V. Kirsanov and N. G. Feshchenko

Dimethyl and diphenyl esters of o-, m- and p-aminophenylsulfonamidophosphoric acid (N^1-phosphates of aminobenzenesulfonamide) were obtained according to the scheme

$$NO_2C_6H_4SO_2NH_2 \xrightarrow[PCl_5]{} NO_2C_6H_4SO_2N{=}PCl_3 \xrightarrow[HCOOH]{}$$
$$\rightarrow NO_2C_6H_4SO_2NHPOCl_2\,[^1] \xrightarrow[2NaOR]{} NO_2C_6H_4SO_2NHPO(OR)_2\,[^2] \xrightarrow[6H]{}$$
$$\rightarrow NH_2C_6H_4SO_2NHPO(OR)_2.$$

Reduction of the diesters of nitrophenylsulfonamidophosphoric acid was carried out with molecular hydrogen in the presence of a platinum catalyst in alcohol solution at room temperature and a pressure of about 100 mm Hg. The yields were quantitative.

The dimethyl and diphenyl esters of aminophenylsulfonamidophosphoric acids (I) were colorless crystalline substances with weak basic and strongly acid properties. They dissolved easily in aqueous soda solutions, titrated as monobasic acids, and their water solutions were acid to Congo paper.

The dimethyl esters of aminophenylsulfonamidophosphoric acids were easily soluble in hot water and were diazotized under ordinary conditions (like aniline). The diphenyl esters dissolved in hot water with difficulty, but easily in alcohol, and were diazotized under the same conditions as aromatic amines with electronegative substituents (for example, nitroaniline).

TABLE 1

Esters of Aminophenylsulfonamidophosphoric Acid $NH_2C_6H_4SO_2NHPO(OR)_2$ (I)

Substance no.	Position of amino group in benzene	R	From what crystallized, crystal form	Melting point	Found			Empirical formula	Calculated*	
					N (%)	OCH_3 (%)	equiv.		N (%)	OCH_3 (%)
(III)	ortho	CH_3	Alcohol, prisms	124—127°	10.27	21.8	1.002	$C_8H_{13}O_5N_2SP$	10.00	22.14
(IV)	meta	CH_3	Water, prisms	192—194	10.28	22.17	1.015	$C_8H_{13}O_5N_2SP$	10.00	22.14
(V)	para	CH_3	Alcohol, needles	146—148	9.9	21.63 22.15	1.007	$C_8H_{13}O_5N_2SP$	10.00	22.14
(VI)	ortho	C_6H_5	Alcohol, needles	166—168	7.14	—	0.980	$C_{18}H_{17}O_5N_2SP$	6.93	—
(VII)	meta	C_6H_5	50% Alcohol, prisms	232—234	7.16	—	0.978	$C_{18}H_{17}O_5N_2SP$	6.93	—
(VIII)	para	C_6H_5	Alcohol, prisms	225—226	6.98	—	1.004	$C_{18}H_{17}O_5N_2SP$	6.93	—

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* Calculated equiv.: 1.0.

TABLE 2

Esters of Benzoylaminophenylsulfonamidophosphoric Acids $C_6H_5CONHC_6H_4SO_2NHPO(OR)_2$ (II)

Substance no.	Position of amino group in benzene ring	R	From what crystallized, form of crystals	Yield (in %)	Melting point	Found			Empirical formula	Calculated*	
						N (%)	OCH$_3$ (%)	equiv.		N (%)	OCH$_3$ (%)
(IX)	ortho	CH_3	Benzene, needles	71.0	151—152°	7.34	15.56, 15.78	0.993	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(X)	meta	CH_3	Alcohol, needles	73.0	171—173	7.31	15.46, 16.00	0.985	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(XI)	para	CH_3	Alcohol, needles	81.0	222—224	7.16	16.07, 15.98	1.003	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(XII)	ortho	C_6H_5	Water, needles	80.0	142—144	5.51	—	1.007	$C_{25}H_{21}O_6N_2SP$	5.51	—
(XIII)	meta	C_6H_5	Alcohol, needles	79.0	206—208	5.65	—	1.002	$C_{25}H_{21}O_6N_2SP$	5.51	—
(XIV)	para	C_6H_5	Alcohol, prisms	86.2	219—221	5.52	—	1.010	$C_{25}H_{21}O_6N_2SP$	5.51	—

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* Calculated equiv.: 1.0.

It is known that amides of o-, m-, and p-aminobenzenesulfonic acids (of which substances (I) are a derivative) melt closely together (153, 142, and 163°, respectively); the meta-isomer is the lowest melting, the para-isomer the highest [3]. In the case of (I) the differences in melting points of ortho-, meta-, and para-isomers is very considerable (see Table 1) and the meta-isomer is the highest melting, the ortho-isomer the lowest. Ortho-isomers of (I) are very easily soluble in acetone at room temperature, the para-isomers dissolve with difficulty on heating, and the meta-isomers are practically insoluble in acetone. Probably the changed melting points and great differences in acetone solubility are explained by the formation of intra- and intermolecular hydrogen bonds for ortho- and para-isomers, respectively, while these are formed with difficulty or not at all for the meta-isomers. The effect of hydrogen bonds on the melting points of aminobenzenesulfonamides is very much less because of the absence of polarizing effect of the phosphoric acid residue, and so they melt more closely together.

We characterized substances (I) by obtaining their benzoyl derivatives by the Schotten-Bauman reaction. They are colorless, crystalline substances with strong acid properties and no basic properties. Their water solutions have an acid reaction to Congo paper. Their melting points in some cases are higher and in some cases lower than the melting points of the corresponding (I) substances. For the other properties of substances (I) and (II), see the experimental part and Tables 1 and 2.

EXPERIMENTAL

General method of obtaining esters of aminophenylsulfonamidophosphoric acid (I). 0.01 mole of the corresponding diester of nitrophenylsulfonamidophosphoric acid [2] was dissolved with heat in 50.0 ml of 96% alcohol and the solution was quickly cooled with energetic stirring so that the nitrocompound crystallized in the smallest possible crystals. We added 0.1 g of platinum oxide [4] and carried out the reduction with hydrogen at a pressure of about 100 mm Hg with continuous shaking. Reduction at first went rapidly accompanied by strong heating and therefore the reaction mixture had to be cooled with ice. During the reduction the nitrocompound gradually dissolved. In some cases near the end of the reaction, substance (I) began to crystallize out. After 1-2 hrs, the theoretical amount of hydrogen had been absorbed and reduction stopped. In the case of substances (III, V, VI) at the end of the reduction the platinum was filtered off, and the alcohol was evaporated in a vacuum on the water bath; the residue was recrystallized from alcohol. In the case of substances (IV), (VII), and (VIII) the reaction products were filtered along with the platinum and then recrystallized: (IV) from boiling water, (VII) from 50% alcohol, and (VIII) from 96% alcohol (1.0 g per 250 ml alcohol). Yields were quantitative. All substances (I) were insoluble in benzene, CCl_4, petroleum ether, and ether. For the solubility in acetone, see above.

Esters of benzoylaminophenylsulfonamidophosphoric acid (II). A mixture of 0.002 g-molecules of the corresponding (I), 2.0 ml of 1 N sodium hydroxide solution, 2.0 ml of 2 N soda solution, and 0.003 g-molecules of benzoyl chloride were energetically shaken until the odor of benzoyl chloride vanished (30-40 min). Then the solution was acidified with 2 N hydrochloric acid. (XI) and (XIV) precipitated directly in the crystalline state, and the other substances (II) came down as thick oils which quickly crystallized completely. To remove the benzoic acid,(IX) was washed with ether (3 × 3.0 ml) and all the other substances (II) were washed with boiling water (4 × 3.0 ml). In boiling water (IX) was easily soluble, (X-XII) were soluble with difficulty, (XIII) with great difficulty, and (XIV) was insoluble. In cold alcohol (IX) and (XII) dissolved easily, (X), (XIII) and (XIV) dissolved in boiling alcohol, and (XI) was difficultly soluble in boiling alcohol. (X), (XI),(XIII), and (XIV) were insoluble in benzene, CCl_4 and ether; (XII) was easily soluble in cold benzene, and (IX) in boiling benzene. (XII) was easily soluble in boiling CCl_4, (IX) dissolved with difficulty. (XII) dissolved easily in cold ether, (IX) was insoluble. None of substances (II) dissolved in petroleum ether. (IX) and (XII) dissolved easily at room temperature in acetone, (XIII) and (XIV) dissolved with somewhat more difficulty, and (X) and (XI) were little soluble in boiling acetone. Thus the ortho derivatives of substances (II) were the most soluble in the majority of organic solvents, and also were the lowest melting; after them came the meta-isomers, and then the para-isomers. Evidently, the effect of intramolecular hydrogen bonds in the ortho-isomers of substances II is the same as in substances (I), but the effect of intermolecular bonds in the para-isomers is almost nonexistent, probably because of blocking of the hydrogen atoms on N^4 by the benzoyl group (compare with melting points and solubilities of substances (I)).

SUMMARY

We have obtained dimethyl and diphenyl esters of aminophenylsulfonamidophosphoric acids and the corresponding benzoylaminophenylsulfonamidophosphoric acids.

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Received February 14, 1957

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* Original Russian pagination. See C. B. translation.

** In Russian.

TRIARYLOXYPHOSPHAZOSULFONALKYLS AND AROMATIC ESTERS OF ALKYL SULFONAMIDOPHOSPHORIC ACIDS

A. V. Kirsanov and N. L. Egorova

Triaryloxyphosphazosulfonalkyls were obtained by the action of sodium arylates with trichlorophosphazosulfonalkyls [1] in a benzene medium according to the scheme

$$RSO_2N{=}PCl_3 + 3ArONa$$

Sodium phenolate and sodium p-chlorophenolate react very energetically with trichlorophosphazosulfonalkyls. The reaction with dry sodium phenolate in the absence of a solvent is very violent and the reaction mixture carbonizes. In the presence of solvent reaction is quiet. Sodium p-nitrophenolate reacts less energetically; reaction proceeds when the mixture is heated on the water bath for 2-3 hrs. In Table 1 we give the yields, melting points, and analytical data for the resulting triaryloxyphosphazosulfonalkyls.

Substances I are all colorless crystals except II, without odor or taste, except for VI which has an intensely bitter taste. When the reaction mixtures are treated with water, all substances I except II precipitate as light, colorless, rectangular plates. They are all easily soluble in acetone, dioxane, and with somewhat greater difficulty in benzene (especially VI), ether and alcohol. They are soluble in boiling carbon tetrachloride and petroleum ether, insoluble in cold water, and only slightly soluble in boiling water. In their physical and chemical properties substances I are very similar to the triaryloxyphosazosulfonaryls [2], but differ somewhat in their greater solubility in boiling water and polar solvents. They are neutral, stable to water and moist air, except for VI which is very easily hydrolyzed. Even when it is dissolved in 96% alcohol it is completely saponified with formation of the p-dinitrodiphenyl ester of ethylsulfonamidophosphoric acid (IX) and nitrophenol according to the scheme

$$C_2H_5SO_2N{=}P(OC_6H_4NO_2\text{-}p)_3 + H_2O \rightarrow \underset{(IX)}{C_2H_5SO_2NHPO(OC_6H_4NO_2\text{-}p)_2} + p\text{-}NO_2C_6H_4OH.$$

In an alcohol-alkali medium, especially with heat, hydrolysis of VI goes more deeply to form a mixture of products of which IX can be isolated with a yield of not more than 50%. All the other substances I are unchanged when heated with alcohol, but are easily saponified when treated with sodium hydroxide in aqueous alcohol to form salts of the corresponding diaryl esters of alkylsulfonamidophosphoric acid (cf. [2]). With mineral acids the latter give the free diaryl esters of alkylsulfonamidophosphoric acids (VII). In Table 2 we give the yields, melting points, and analytical data for the resulting substances VII. They are colorless, crystalline substances which have a very bitter taste. They are all easily soluble in acetone and hot alcohol, very difficultly soluble in cold water and easily in hot, and difficultly soluble in most nonpolar solvents. Chemically they are strong monobasic acids. The substances VII are considerably more stable to hydrolysis by both acids and alkalis than substances I.

The structure of substances VII is clear not only because they result from saponification of substances I, but also from their synthesis by the reaction of alkylsulfonamidophosphoric acid dichlorides [3] with sodium arylates by the scheme

$$RSO_2NHPOCl_2 + 2ArONa \rightarrow RSO_2NHPO(OAr)_2 + 2NaCl$$

TABLE 1

Triaryloxyphosphazosulfonalkyls of the Type $RSO_2N{=}P(OAr)_3$ (I)

Substance no.	R	Ar	From what crystallized, form of crystals	Yield (in %)	Melting point	Found (%N)	Empirical formula	Calculated (%N)
—	CH_3	C_6H_5	Benzene, needles; ether, cubes	86.2	90—92°	3.48	$C_{19}H_{18}O_5NSP$	3.47
—	C_2H_5	C_6H_5	Benzene, prisms	83.9	100—101	3.37	$C_{20}H_{20}O_5NSP$	3.35
—	iso-C_3H_7	C_6H_5	Petroleum ether, needles	81.2	66—68	3.23	$C_{21}H_{22}O_5NSP$	3.25
(II)	n-C_4H_9	C_6H_5	Liquid d_4^{20} ~ 1.2	85.4	—	2.95	$C_{22}H_{24}O_5NSP$	3.14
(III)	$C_6H_5CH_2$	C_6H_5	Benzene, prisms; water, rectangular plates	86.5	89—90	2.86	$C_{25}H_{22}O_5NSPCl_2$	2.92
(IV)	C_2H_5	p-ClC_6H_4	Benzene, hexahedral prisms; petroleum ether, cubes	74.0	70—72	2.61	$C_{20}H_{17}O_5NSPCl_2$	2.68
(V)	$C_6H_5CH_2$	p-ClC_6H_4	Alcohol, rhombohedra; petroleum ether, cubes	75.5	132—133	2.34	$C_{25}H_{19}O_5NSPCl_3$	2.42
(VI)	C_2H_5	p-$NO_2C_6H_4$	Benzene, fine needles	65.2	108—110	9.90	$C_{20}H_{17}O_{11}N_4SP$	10.10

TABLE 2

Diaryl Esters of Alkylsulfonamidophosphoric Acids of the Type $RSO_2NHPO(OAr)_2$ (VII)

Substance no.	R	Ar	From what crystallized, form of crystals	Yield (in %)	Melting point	Found equiv.	Empirical formula**
—	CH_3	C_6H_5	CCl_4, long needles	43.3	96—98°	0.99, 1.00	$C_{13}H_{14}O_5NSP$
—	C_2H_5	C_6H_5	CCl_4, fine prisms	77.2	117—119	1.01, 1.01	$C_{14}H_{16}O_5NSP$
—	iso-C_3H_7	C_6H_5	CCl_4, fine prisms	86.3	140—142	1.01, 0.99	$C_{15}H_{18}O_5NSP$
—	n-C_4H_9	C_6H_5	CCl_4, fine needles	76.7	109—110	0.98, 1.00	$C_{16}H_{20}O_5NSP$
—	$C_6H_5CH_2$	C_6H_5	Water (precipitate), fine prisms	89.3	147—148	1.00, 1.00	$C_{19}H_{18}O_5NSP$
VIII	CH_3	p-ClC_6H_4	Ether, Rhombohedra	72.3 *	58—60	1.07, 1.06	$C_{13}H_{12}O_5NSPCl_2$
—	C_2H_5	p-ClC_6H_4	Water (precipitate), rectangular plates	90.0	133—135	1.01, 1.04	$C_{14}H_{14}O_5NSPCl_2$
—	$C_6H_5CH_2$	p-ClC_6H_4	Water (precipitate), fine prisms	73.8 *	149—151	0.99, 1.02	$C_{19}H_{16}O_5NSPCl_2$
IX	C_2H_5	p-$NO_2C_6H_4$	Alcohol, long prisms	78.9	166—167	0.98, 1.00	$C_{14}H_{14}O_9N_3SP$

* Yields from the synthesis from the dichlorides of the corresponding alkylsulfonamidophosphoric acids. All other yields for preparation by saponification of substances (I).

** Calculated equiv.: 1.0.

EXPERIMENTAL

General method for preparing triaryloxyphosphazosulfonalkyls (I). 0.03 g-molecules of carefully dried and ground sodium phenolate was moistened with 5 ml of dry benzene and a solution of 0.01 g-molecule of the corresponding trichlorophosphazosulfonalkyl in 20 ml of benzene was added with stirring. To complete the reaction, the mixture was heated on the boiling water bath for 30 min. In preparing (V) the heating lasted 4 hrs, and for (VI), 2 hrs. The benzene was distilled off in a vacuum and the syrupy residue was treated with 80-100 ml of water. With this treatment, all the substances (I) precipitated as heavy colorless rectangular plates which were filtered, washed with water, dried, and recrystallized (see Table 1). (II) precipitated as a thick oil which was extracted with benzene. The benzene extract was washed with 0.5 N sodium hydroxide solution, dried over sodium sulfate, and the benzene was distilled off in a vacuum at 50°. It was also possible after the reaction had been carried out to filter out the sodium chloride and distill off most of the benzene in a vacuum. When the solution was cooled, all the substances (I) precipitated as crystals (needles or prisms). This method was particularly suitable for (VI) which was difficultly soluble in cold benzene, and also for (III) and (IV).

General method for preparing diaryl esters of alkylsulfonamidophosphoric acids (X) by saponification of (I). A mixture of 0.01 g-molecule of the corresponding (I), 100 ml of alcohol, and 40 ml of 1 N aqueous solution of sodium hydroxide was heated on the water bath for 1 hr. The alcohol was distilled off in a vacuum, the water solution was filtered, and hydrochloric acid was added to an acid reaction to Congo paper. Substances (VII) then precipitated; they were filtered, dried, and, if necessary, recrystallized (see Table 2).

(IX) was obtained by boiling a solution of 0.003 g-molecule of (VI) in 30.0 ml of 96% alcohol for 10 min. The alcohol was distilled off in a vacuum, and the crystalline precipitate was washed with water and ether.

General method for preparing diaryl ethers of alkylsulfonamidophosphoric acids from alkylsulfonamidophosphoric acid dichlorides and sodium arylates. To a solution of 0.01 g-molecule of the dichloride of the corresponding alkylsulfonamidophosphoric acid in 100 ml of benzene was added 0.03 g-molecule of sodium arylate and the mixture was heated to boiling for 1 hr under reflux. The benzene was distilled off in a vacuum on a boiling water bath, the residue was dissolved in water, the solution was filtered and acidified with hydrochloric acid to an acid reaction to Congo. Substances (VII) precipitated and were filtered, washed with water, and dried. Substances (VII) obtained in this manner were usually entirely pure and did not have to be recrystallized. (VIII) which was comparatively easily soluble in water was extracted by ether after addition of acid.

SUMMARY

We have obtained triaryloxyphosphazosulfonalkyls and diaryl esters of alkylsulfonamidophosphoric acids and described their properties.

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Received February 4, 1957

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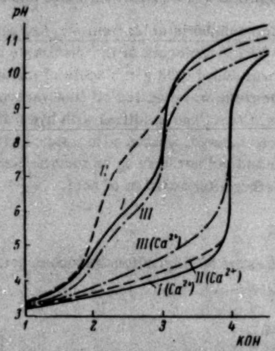
* Original Russian pagination. See C. B. translation.

SUBSTANCES WITH COMPLEX FORMING ABILITY

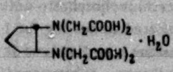
II. TRANS-1,2-DIAMINOCYCLOPENTANE-N,N,N',N'-TETRAACETIC ACID AND TRANS-1,2-DIAMINOCYCLOBUTANE-N,N,N',N'-TETRAACETIC ACID

V. G. Iashunskii

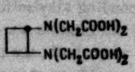
In a previous communication [1] we showed that the widely known "Complexon-IV," 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (I) has a trans-configuration. In order to study the effect of the structure of complexons on their complex forming power, we synthesized the undescribed close analogs of (I), trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid (II) and trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid (III). Acid (II) crystallizes with 1 molecule of water of crystallization which is not removed by heating in a vacuum to 100°. Acid (III) contains no water of crystallization.



Curve of potentiometric titration of the tetra-acids (I), (II), and (III) in absence and presence of Ca^{2+} ions (amount of KOH in g-moles per 1 g-mole of tetra-acid).



(II)



(III)

Both tetra-acids were obtained by condensation of the corresponding diamino dihydrochlorides with monochloroacetic acid in the presence of alkali. Trans-1,2-diaminocyclopentane dihydrochloride was synthesized starting from ethyl cyclopentanone-2-carboxylate by nitration, oxime formation, and reduction of the resulting dioxime with metallic sodium in alcohol [2]. Trans-1,2-diaminocyclobutane dihydrochloride was obtained by the Curtius reaction from the dihydrazide of trans-cyclobutane-1,2-dicarboxylic acid, which was prepared from the corresponding diester [3].

Potentiometric titration of both tetra-acids in the absence and presence of calcium ions showed that these complexons resembled (I) in properties and also gave simple internal complex compounds, especially with Ca, of the composition CaX^{2-} (X is the tetra-acid residue). In the figure we give the curves for the potentiometric titration of (II) and (III), and for comparison, of (I). The data of the potentiometric titrations allows us to calculate [1] the apparent dissociation constants and stability constants of the Ca complexes of the complexons which we synthesized. In Table 1 for comparison we give also the corresponding values for (I) and for ethylenediamine-N,N,N',N'-tetraacetic acid (IV).

The results allow us to draw some conclusions as to the effect of structure of these complexons on ability to form complexes. If we compare the values of the stability constants of the Ca complexes of (IV), (I),(II), and (III), we can assume that to a large extent, two factors allow an increased stability of similar inner complex metallo-rings: closeness of the amino groups in the diamine molecule and absence of free rotation of these relative to the C_1-C_2 bond. In (IV) there is the maximum possible closeness of amino groups, but limitation of free rotation is absent. In (I) the cyclohexane ring permits closeness of the amino groups; the possibility of shifting of these

TABLE 1

Complexons	Reciprocal of logarithm of apparent dissociation constant				Logarithm of stability constant of Ca complex
	pK_1	pK_2	pK_3	pK_4	
(I)	2.7	3.6	6.15	11.65	12.5
(II)	2.4	3.3	7.56	10.80	12.2
(III)	2.7	2.8	5.80	9.75	8.0
(IV)*	1.996	2.672	6.161	10.262	10.59

* Data taken from the work of Schwarzenbach and Ackermann [4].

groups relative to each other is considerably decreased, but it does occur, since the six-membered ring can exist in the form of the "bath" and the "chair." Actually, the stability of the Ca complex of (I) compared to that of (IV) is considerably increased. In (II) the plane of the cyclopentane ring allows a distance of the amino groups from each other, but they become firmly held. As the experimental data with Ca^{2+} show, (I) and (II) have about the same complex forming ability. In (III) we find a still greater distance for the amino groups, and the absence of any free rotation. The potentiometric titration in the presence of Ca^{2+} shows that the value of the stability constant for the Ca complex of (III) is considerably lower than for (I) and even for (IV).

In a later study we shall investigate these regularities in the cis-series.

EXPERIMENTAL

Trans-cyclobutane-1,2-carboxylic acid dihydrazide [3]. 9.15 g of diethyl trans-cyclobutane-1,2-dicarboxylate (b. p. 126-127° at 17 mm, $d^{20}D$ 1.4406) was heated with 11.2 of hydrazine hydrate for 8 hrs at 130-135°. The resulting precipitate was treated with hot anhydrous ethyl alcohol and after cooling, this was filtered. After recrystallization from 50% ethyl alcohol, 5.65 g of the hydrazide was obtained, melting at 221-222°.

Trans-1,2-diaminocyclobutane dihydrochloride. 5.25 g of the dihydrazide was dissolved in 21 ml of 10% hydrochloric acid, 60 ml of ether was added, and with stirring at 18-20° a solution of 4.2 g of sodium nitrite in 9 ml of water was gradually added. The ether layer was separated, the water layer was twice extracted with 20 ml of ether, and after the ether solution was dried for 10-15 min over calcium chloride, 30 ml of anhydrous ethyl

TABLE 2

Tetraacid (II)			Tetraacid (III)		
KOH (mole/1 mole II)	conc. ($\times 10^{-4}$)	[H]	KOH(mole per mole III)	conc. ($\times 10^{-4}$)	[H]
0.427	9.92	$1.15 \cdot 10^{-3}$	1.372	9.99	$5.01 \cdot 10^{-4}$
0.854	9.88	$6.92 \cdot 10^{-4}$	1.476	9.98	$3.98 \cdot 10^{-4}$
0.960	9.87	$6.03 \cdot 10^{-4}$	1.580	9.97	$3.24 \cdot 10^{-4}$
1.068	9.86	$5.01 \cdot 10^{-4}$			
Titration in presence of Ca^{2+} (0.01 M)					
2.695	9.84	$6.31 \cdot 10^{-5}$	2.762	9.76	$1.95 \cdot 10^{-5}$
2.802	9.83	$6.03 \cdot 10^{-5}$	2.975	9.73	$1.38 \cdot 10^{-5}$
2.908	9.82	$5.01 \cdot 10^{-5}$	3.185	9.72	$9.33 \cdot 10^{-6}$

Note. Titration was carried out with 0.1 N KOH at 20° ($\mu = 0.1$). $pK_3' + pK_4' = 8.1$ for tetra-acid (II) and $pK_3' + pK_4' = 9.5$ for tetra-acid (III).

alcohol was added. The ether was distilled off and the residue was heated to boiling for 1 hr; then 25 g of potassium hydroxide and 75 ml of methyl alcohol were added and boiling was continued for 2 hrs more. The mixture was then distilled with steam, the distillate was acidified with hydrochloric acid and evaporated dry. We obtained 3.18 g (67%) of trans-1,2-diaminocyclobutane dihyrochloride which was recrystallized from hydrochloric acid.

Found %: Cl 44.62. $C_4H_{10}N_2 \cdot 2HCl$. Calculated %: Cl 44.57.

Trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid. To 8.9 g of monochloroacetic acid neutralized with 13.5 ml of 7 N sodium hydroxide solution we added 3.0 g of trans-1,2-diaminocyclobutane dihydrochloride: the mixture was heated on the boiling water bath and 18 ml of 7 N sodium hydroxide solution was added with stirring. The addition of alkali was so conducted that tests constantly gave a blue color on thymolphthalein paper. After 3 hrs the mixture was acidified with concentrated hydrochloric acid to a pH of 1-2, and the precipitate was recrystallized from a large amount of water. We obtained 2.83 g of pure tetra-acid.

Found %: C 45.13; H 5.71; N 8.86. M 318.1 (on titration with $CaCl_2$ in the presence of murexide). $C_{12}H_{18}O_8N_2$. Calculated %: C 45.28; H 5.70; N 8.80. M 318.3.

Trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid was obtained in a manner analogous to the above from trans-1,2-diaminocyclopentane dihydrochloride; the yield after reprecipitating the acid from alkaline solution was 56%.

Found %: C 44.76; H 6.25; N 8.27. M 349.6 (on titration with $CaCl_2$ in the presence of murexide). $C_{13}H_{20}O_8N_2 \cdot H_2O$. Calculated %: C 44.56; H 6.33; N 8.00. M 350.3.

When it was heated in a vacuum to 100° the monohydrate did not lose a molecule of water. Potentiometric determination and calculation of dissociation constants was carried out by the method of Schwarzenbach (see [1]). As an example, in Table 2 we give the results of one of the parallel titrations for the tetra-acids (II) and (III).

SUMMARY

We have synthesized the previously undescribed complexons: trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid and trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid for which we determined the apparent dissociation constants and the stability of the Ca complexes.

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Received February 7, 1957

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* Original Russian pagination. See C. B. translation.

CYANOETHYLATION OF ARYL SULFONAMIDES

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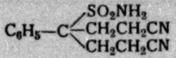
The study of the chemical properties of benzenesulfonamide and its derivatives has great interest for the discovery of new sulfonamide compounds and for an explanation of their pharmacological action [1]. In recent times the cyanoethylation reaction has been widely used, taking place when acrylonitrile acts on substances with a mobile hydrogen atom. A series of reviews on cyanoethylation have appeared [2]. Acrylonitrile has acted on halides, amines, compounds of the type of malonic ester, and others. There have been studies on cyanoethylation of acids and their derivatives, esters, nitriles, and amides [3-5]. The synthetic possibilities of this reaction have only been touched upon, but already the opportunities for its practical use are clear.

The literature mentions that when the products of cyanoethylation of amines are hydrolyzed, substances are obtained which have physiological activity [6, 7]. As is known, the most active sulfonamides contain the benzenesulfonamide grouping with substitution of the hydrogen atoms in the amide group [8]; therefore we studied the cyanoethylation reaction of benzenesulfonamide and its derivatives.

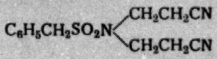
Benzenesulfonamide in the presence of alkaline agents reacts with acrylonitrile at 100° to form the dicyanoethyl derivative [9, 10].

Among the substituted benzenesulfonamides, to judge them from the literature data, benzylsulfonamide is cyanoethylated. The resulting product was assigned structure (I) [5]. However, as was shown later [11] cyanoethylation occurs on the amide group with formation of compound (II).



$$C_6H_5-C\begin{cases}SO_2NH_2\\CH_2CH_2CN\\CH_2CH_2CN\end{cases}$$

(I)

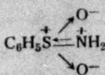


$$C_6H_5CH_2SO_2N\begin{cases}CH_2CH_2CN\\CH_2CH_2CN\end{cases}$$

(II)

The mechanism of reaction of combining acrylonitrile with benzenesulfonamide and its derivatives differs from the mechanism of cyanoethylation of the amides of carboxylic acids [12]. The latter react sluggishly with acrylonitrile. Thus, acetamide in the presence of alkali gives products of mono- and dicyanoethylation on the amide group [9, 10]. It is interesting to observe that with heat the dicyanoethyl derivatives with acetamide disproportionate with formation of monocyanoethyl compounds in 62% yield [9].

When benzenesulfonamide undergoes cyanoethylation it is important to consider the combination of the benzene ring with sulfo- and amino groups. A positive charge occurs on the nitrogen atom as a result of the electrophilic action of the sulfur atom and the shift of free electrons; this makes detachment of the proton easy (A).



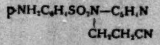
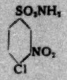
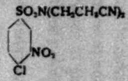
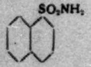
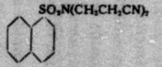
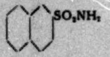
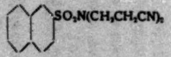
$$C_6H_5\overset{+}{S}\begin{cases}\nearrow O^-\\ \leftarrow \overset{+}{N}H_2\\ \searrow O^-\end{cases}$$

(A)

This splitting is stronger in an alkaline medium where a state of dynamic equilibrium is established.

$$C_6H_5SO_2NH_2+2Na^+ + 2(OH)^- \rightleftarrows [C_6H_5SO_2\ddot{N}:]^= + 2Na^+ +$$
$$+ 2(OH)^- + 2H^+ \rightleftarrows [C_6H_5SO_2\ddot{N}:]^= + 2Na^+ + H_2O.$$

Cyanoethylation of Arylsulfonamides

Starting substance	Resulting substance	Melting point	Kjeldahl nitrogen analysis [13]		Yield (in %)	Catalyst
			found	calc.		
$C_6H_5SO_2NH_2$	$C_6H_5SO_2N(CH_2CH_2CN)_2$	92°	16.71	15.96	66.2	NaOH
$p\text{-}CH_3C_6H_4SO_2NH_2$	$p\text{-}CH_3C_6H_4SO_2N(CH_2CH_2CN)_2$	104—105	15.09	15.16	77.3	NaOH
	$p\text{-}CH_3C_6H_4SO_2NHCH_2CH_2CN$	55—56			15.7	
$p\text{-}ClC_6H_4SO_2NH_2$	$p\text{-}ClC_6H_4SO_2N(CH_2CH_2CN)_2$	133	13.5	14.1	70	NaOH
$p\text{-}NH_2C_6H_4SO_2NH_2$	$p\text{-}NH_2C_6H_4SO_2N(CH_2CH_2CN)_2$	145	20.1	20.14	57.7 66.9	NaOH Rodionov Catalyst
$p\text{-}CH_3CONHC_6H_4SO_2NH_2$	$p\text{-}CH_3CONHC_6H_4SO_2N(CH_2CH_2CN)_2$	131—132	17.66	17.46	75	Rodionov Catalyst
$p\text{-}NH_2C_6H_4SO_2NHC_5H_4N$	 $p\text{-}NH_2C_6H_4SO_2\underset{CH_2CH_2CN}{\underset{\vert}{N}}\text{—}C_5H_4N$	165	18.23	18.54	73	Rodionov Catalyst
$p\text{-}NO_2C_6H_4SO_2NH_2$	$p\text{-}NO_2C_6H_4SO_2N(CH_2CH_2CN)_2$	150			67.8	NaOH
		160—162			64.3	NaOH
		152	13.36	12.84	65.1	NaOH
		210	13.33	12.84	58.4	NaOH

Spectrographic study of benzenesulfonamide in an alkaline medium at ratio of molar concentrations 2 : 1 shows the splitting of two protons and formation of a doubly charged anion of benzenesulfonamide $[C_6H_5SO_2\underset{..}{\overset{..}{N}}:]^{=}$ [1]. This evidently explains the catalytic action of the sodium hydroxide on the cyanoethylation of benzenesulfonamide and also the difficulty of isolating the products of monocyanoethylation. At a molar ratio of benzenesulfonamide and sodium hydroxide of 1 : 3 under our conditions it is possible also to form the singly charged anion of benzenesulfonamide $[C_6H_5SO_2NH]^{-}$.

The reaction of cyanoethylation of benzenesulfonamide was carried out as follows. 5.2 g of benzenesulfonamide dissolved in 20 ml of dioxane was heated with 0.5 g of sodium hydroxide on the water bath under reflux, with gradual addition of 5 ml of acrylonitrile. Heating was continued 1.5-2 hrs and the reaction mixture allowed to stand for a day. The dicyanoethylation product was easily isolated after decomposition of the reaction mixture with water. Dicyanoethylbenzenesulfonamide recrystallized from ethanol appeared as white needles, melting at 92°. If the solvent (dioxane) was distilled from the reaction mixture in a vacuum, then along with the dicyanoethylbenzenesulfonamide we obtained a small amount of an oil which crystallized when it stood in a vacuum desiccator over sulfuric acid. When the cyanoethylation reaction was carried out in anhydrous ethanol, the amount of this oil increased.

We carried out cyanoethylation of the following derivatives of benzenesulfonamide with nucleophilic substituents: p-toluenesulfonamide, p-chlorobenzenesulfonamide, p-aminobenzenesulfonamide, p-acetylaminobenzenesulfonamide, and sulfidine. The resulting cyanoethylated derivatives of benzenesulfonamide and their analytical data are shown in the table.

The cyanoethylation reaction with p-toluenesulfonamide was carried out in dioxane and ethanol solutions under the conditions for cyanoethylation of benzenesulfonamide. After 4 hr heating of the reaction mixture in ethanol solution we obtained the products of di- and monocyanoethylation of p-toluenesulfonamide. The monocyanoethylation product was easily separated and formed in greater yield than in the case of benzenesulfonamide. This was explained by the effect of the methyl group on the union of the sulfonamide group with the benzene ring and the greater possibility of forming a singly charged anion of benzenesulfonamide.

When p-toluenesulfonamide and its dicyanoethylation product were heated in anhydrous alcohol in the presence of sodium hydroxide, a disproportionation reaction occurred and the product of monocyanoethylation of p-toluenesulfonamide, melting 55-56°, was formed.

For the cyanoethylation of p-aminobenzenesulfonamide we used sodium hydroxide and the Rodionov catalyst as catalysts; the latter we obtained from methyl p-aminobenzenesulfonate [14]. In both cases we obtained the same dicyanoethylation product, but with the Rodionov catalyst reaction occurred more smoothly and the yield was higher. Analysis for nitrogen showed that two atoms of hydrogen were cyanoethylated in the molecule of p-aminobenzenesulfonamide. To establish the mechanism of the reaction, which in this case might have occurred on the amido or the amino group, we cyanoethylated substituted benzenesulfonamides, the acetylated streptocide and sulfidine, in pyridine solution (see table).

Cyanoethylation of p-aminobenzene-N-dimethylsulfonamide showed that reaction did not occur under these conditions.

p-Aminobenzene-N-dimethylsulfonamide was prepared by reduction of p-nitrobenzenedimethylsulfonamide [15].

The N-methylamide of acetylsulfanilic acid, $CH_3CONHC_6H_4SO_2NHCH_3$, was cyanoethylated on the sulfonamide group, but the N,N-dimethyl amide of acetylsulfanilic acid $CH_3CONHC_6H_4SO_2N(CH_3)_2$ did not cyanoethylate. Cyanoethylation does not occur on the carbamide group [16].

Among the derivatives of benzenesulfonamide with electrophilic substituents we cyanoethylated p-nitrobenzenesulfonamide, prepared from p-nitrochlorobenzene [17, 18]. Reaction was carried out in dioxane in the presence of the Rodionov catalyst with longer heating of the reaction mixture.

The literature describes a series of cyanoethylation products of chlorine substituted aromatic compounds, which were investigated as insecticides [19]. Because of this interest we prepared 1-chloro-2-nitro-4-benzenesulfonamide. Strong reaction occurred in the presence of Rodionov catalyst with formation of the dicyanoethylation product.

SUMMARY

1. In the cyanoethylation reaction with acrylonitrile we have obtained 10 new compounds, not described in the literature.

2. A study of the mechanism of this reaction shows that replacement of hydrogens by the cyanoethyl group under the conditions described occurs only on the amide group. Reaction does not occur on the amino group.

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Received March 26, 1957

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** In Russian.

SYNTHESIS OF THE DIETHYLENEIMIDE OF 4-METHYLURACIL 5-METHYLENE PHOSPHINIC ACID

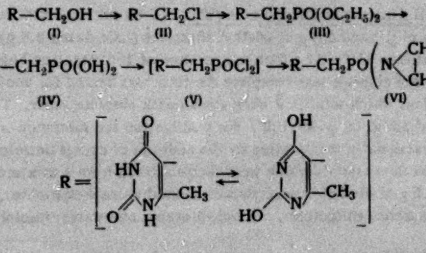
A. Ia. Berlin and M. N. Vasil'eva

In seeking new chemical agents against malignant neoplasms the attention of many investigations has turned to substances with so-called "alkylating" action, substances which contain β,β'-dichlorodiethylamino and ethylene imino groups, etc.

The recently synthesized p-(β,β'-dichlorodiethylamino)-phenylalanine hydrochloride ("sarcolysine") [1] is one of the most interesting preparations of this type, since its clinical use has for the first time permitted effective action against some forms of true human tumors and their metastases [2]. In the sarcolysine molecule there is an active alkylating dichlorodiethylamino group combined with a phenylalanine residue which plays an important part in protein metabolism. This fact leads us to seek a substance with analogous structural characteristics which might have an anti-cancer action also for other types of malignant tumors.

Starting from these ideas, we were interested in synthesizing the diethylene imide of 4-methyluracil 5-methylenephosphinic acid (VI), which contains the active cytotoxic diethylenephosphoramide group along with a residue of a uracil derivative which, like some of its other derivatives, enters the composition of nucleic acids.

The synthesis was carried out according to the following scheme.


R—CH₂OH → R—CH₂Cl → R—CH₂PO(OC₂H₅)₂ →
(I)
(II)
(III)
→ R—CH₂PO(OH)₂ → [R—CH₂POCl₂] → R—CH₂PO(N<CH₂,CH₂)₂
(IV)
(V)
(VI)
R =
HN
N
H
O
O
CH₃
⇄
OH
N
N
HO
CH₃

The transformation of 4-methyl-5-hydroxymethyluracil ("pentoxyl") (I) into the corresponding chloride (II) required careful choice of reaction conditions, since the chlorine could replace not only the hydroxyl group in the side chain but also the hydroxyl of the lactone form of the uracil ring [3]. It was shown that the best method was to carry out reaction between pentoxyl and thionyl chloride in cold chloroform in the presence of 1 mole of pyridine. Excess pyridine caused considerable tarring.

The resulting 4-methyl-5-chloromethyluracil (II) melted about 225° (with decomposition) with a rate of heating of 10° per minute. With slower heating (2° per min) the substance gradually darkened but did not melt up to 345°. Endicott and Johnson [4] synthesized this compound from 4-methyluracil and monochloromethyl ether; without mentioning the effect of rate of heating on melting point, they observed that it turned yellow at 225° and melted with decomposition at 330-335°. We can assume that Endicott and Johnson apparently had the same substance but determined its melting point with a different rate of heating. It should be remarked that the melting point given by Johnson and Chernoff [5] for the isomeric 4-chloromethyl-5-methyluracil, 243°, is close to that established by us for substance (II). When we repeated the synthesis described by Endicott and Johnson [4] we obtained a complex mixture of substances which easily altered, and which was very difficult to separate. This led us to work out the other synthesis of (II) starting with pentoxyl.

Next, by the action of triethyl phosphite on 4-methyl-5-chloromethyluracil (II), by the Arbuzov reaction, we isolated the diethyl ester of 4-methyluracil 5-methylenephosphinic acid (III). Heating the diethyl ester (III) with hydrochloric acid gave a good yield of the corresponding 4-methyluracil 5-methylenephosphinic acid (IV).

The transformation of the phosphinic acid (IV) into its dichloride (V) also required care in carrying out the reaction in view of the above-mentioned possibility of undesired substitution. However, even with very mild conditions the reaction does not go in a single direction and a mixture of different substances results, from which we were unable to separate the chloride (V) in pure form. Nonetheless, the fact of formation of 4-methyluracil 5-methylenephosphinic acid dichloride was established, since reaction of the mixture of substances with anhydrous ethyl alcohol gave 21% of the diethyl ester (III) (after recrystallization).

Analogously, the action of ethylene imine on the reaction product from the phosphinic acid (IV) and thionyl chloride [6] gave the diethylene imide of 4-methyluracil 5-methylenephosphinic acid (VI) as a crystalline substance which changed when heated in a capillary but showed no definite melting point.

We consider it a pleasure to express our gratitude to M. I. Kabachnik and T. Ia. Medved for their advice in our work.

EXPERIMENTAL

4-Methyl-5-chloromethyluracil (II). To a mixture of 10 g of 4-methyl-5-hydroxymethyluracil (pentoxyl), 5.1 ml of dry pyridine and 100 ml of dry chloroform was added a solution of 10 g of thionyl chloride in 15 ml of the same solvent over a period of 30 min with stirring and ice cooling. The reaction temperature did not exceed 20°. After 3 hrs of stirring, the reaction mixture was filtered, the precipitate was well washed with dry chloroform and air dried until the odor of SO_2 vanished. Weight 8 g. After 3 recrystallizations from dioxane we obtained 5.1 g of crystalline substance melting at ~ 225° (with decomposition) with a rate of heating of 10° per min.

Found %: C 41.2, 41.5; H 4.2, 4.2; N 16.5, 16.5; Cl 20.2, 20.4. $C_6H_7O_2N_2Cl$. Calculated %: C 41.2; H 4.0; N 16.0; Cl 20.4.[*]

Diethyl 4-methyluracil 5-methylenephosphinate (III). In a 50 ml flask with reflux condenser and calcium chloride tube was placed 4 g of (II) and 4.3 g of triethyl phosphite (calculated 3.8 g). The mixture was placed in an oil bath previously heated to 130°. At a bath temperature of 160° reaction began with a violent evolution of gas. When evolution of ethyl chloride was complete the flask was heated for another 20 min at 150-155°. The result of the reaction was an oil which solidified when stirred with absolute ether. The solid mass was well washed with ether and dried. Weight 3.8 g, m. p. 97-102°. For purification the substance was dissolved in 12.0 ml of dry benzene at 40-55° and fractionally precipitated by the addition of excess petroleum ether. An oily substance first began to precipitate, and then crystals which were recrystallized from a mixture of benzene and petroleum ether (4 : 1). We obtained 2.2 g of diethyl 4-methyluracil 5-methylenephosphinate., m. p. 106-107.5°. The substance was well soluble in benzene, chloroform, alcohol, dioxane, and water; insoluble in ether and petroleum ether.

Found %: C 43.5, 43.3; H 6.2, 6.5; N 9.8, 10.1; P 11.06, 11.02. $C_{10}H_{17}O_5N_2P$. Calculated %: C 43.5; H 6.2; N 10.2; P 11.2.

4-Methyluracil 5-methylenephosphinic acid (IV). 0.5 g (III) in 10 ml of concentrated hydrochloric acid was boiled for 5 hrs. After removal of excess hydrochloric acid in a vacuum we obtained 0.4 g of 4-methyluracil 5-methylenephosphinic acid, m. p. 280°. It was recrystallized from dilute ethyl alcohol to give 0.3 g (IV) with m. p. 282-284°.

Found %: C 32.5, 32.5; H 4.1, 4.1. $C_6H_9O_5N_2P$. Calculated %: C 32.7; H 4.1.

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[*] All the analyses were carried out in the Analytical Chemistry Laboratory of our Institute.

Diethylene imide of 4-methyluracil 5-methylenephosphonic acid (VI). 5 g of (IV) in 50 ml of thionyl chloride was heated at 50° for 30 min. After removing the excess thionyl chloride in a vacuum at room temperature, the dry residue was treated with 50 ml of dry benzene. A solution of 2.5 ml of ethylene imine and 7.5 ml of triethylamine in 20 ml of dry benzene was added from a dropping funnel with stirring. The flask was then cooled with ice water so that the bath temperature did not exceed 10°. After all the solution had been added, the mixture was stirred for 2.5 hrs more and allowed to stand for 16 hrs at 0-5°. The precipitate was filtered off. The solvent was removed from the filtrate in a vacuum in a stream of nitrogen at a bath temperature not above 30° and the solid residue was recrystallized from dry benzene which was not heated above 45°. We obtained 1.5 g of the diethylene imine of 4-methyluracil 5-methylenephosphinic acid. In the melting point determination the substance began to darken at about 120° and on further heating gradually changed and decomposed at 268°.

Found %: C 44.1, 44.2; H 5.5, 5.6; N 20.1, 20.1. $C_{10}H_{15}O_3N_4P$. Calculated %: C 44.4; H 5.5; N 20.7.

SUMMARY

Starting from 4-methyl-5-hydroxymethyluracil (pentoxyl) through 4-methyl-5-chloromethyluracil we synthesized the diethyl ester of 4-methyluracil 5-methylenephosphinic acid and the free 4-methyluracil 5-methylene phosphinic acid. From the latter we obtained the diethylene imine of 4-methyluracil 5-methylenephosphinic acid.

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Received March 27, 1957

STUDIES IN THE FIELD OF SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

I. SYNTHESIS OF N,N'-DIALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

D. L. Klebanskii and M. S. Vilesova

The value of polyamides for different branches of industry is widely known.

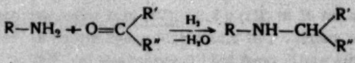
In recent decades, works have begun to appear in the literature concerning the question of modifying the properties of polyamides to give them more elasticity, softness, and hydrophilic properties, while retaining a series of other valuable properties. Such modifications can be brought about by several methods. In particular, the method of N-alkylation has wide possibilities; yet in the literature it has not been sufficiently reported.

To obtain N-alkylated polyamides with varying degrees of substitution and also with different substituted radicals it is necessary to have methods for the synthesis of the corresponding monomers (N-alkylated hexamethylenediamine) which will guarantee a sufficiently pure product, the possibility of introducing radicals with different structures, and also the possibility of preferentially directing the reaction toward N-mono- or symmetrical N,N'-dialkylation. It would also be desirable that the method be simple, based on available compounds and that it permit the carrying out of the reaction on a large scale. Such a method is not now known. Methods are described in the literature for the synthesis of N,N'-dialkyldiamides by amination of the corresponding dibromides [1], and by hydrogenation of the dinitriles in the presence of methylamine [2]. Both methods lead to the formation of a mixture of products which are difficult to separate.

The reduction of Schiff bases of diamines described by Staudinger is complicated by the great instability of the aliphatic azomethines and leads to a low yield of the latter [3].

Since the polycondensation process requires monomers with a high degree of purity, the method of reductive alkylation of amines by aldehydes and ketones is of interest; this, according to the description [4], assures a high yield and a choice of reactions for getting secondary monoamines and satisfies the other requirements discussed above. The literature data relate entirely to monoamines. With regard to the reductive alkylation of diamines there is only one patent, which concerns obtaining N-monoalkyl derivatives [5].

The complexity and peculiarity of the reaction of alkylating diamines is connected with the presence of two active groups in the diamine molecule. In this connection, one of the problems of our investigation is to work out a synthesis of N,N'-dialkyl derivatives of hexamethylene diamine based on reductive alkylation and proceeding according to the following scheme



$$R{-}NH_2 + O{=}C\begin{matrix} R' \\ R'' \end{matrix} \xrightarrow[-H_2O]{H_2} R{-}NH{-}CH\begin{matrix} R' \\ R'' \end{matrix}$$

R' and R" are alkyl radicals or H

We studied the effect of a series of factors on reaction rate and yield of N,N'-dialkyl derivatives of hexamethylene diamine.

Effect of solvents. The reaction carried on without solvent was unsatisfactory, since the exothermic nature of the process caused strong tarring. The viscous consistency of the mixture also prevented even distribution of the catalyst and worsened the conditions of hydrogenation. We used as solvents substances which dissolved both the diamine and the carbonyl compound well. The results are shown in Table 1.

TABLE 1

Effect of Solvents on Course of Reductive Alkylation of Hexamethylenediamine

Alkylating compound	Solvent	Duration of 50% reaction (in min)	Limiting extent of reaction (in %)	Yield of N,N'-dialkyl derivative (in %)
Butyraldehyde	Anhydrous alcohol	15—16	100	87
	96% alcohol	15—17	100	85
	Dioxane	25—30	82	70
	Water	27—30	70	50—55
Acetone	Anhydrous alcohol	8—10	100	96
	96% alcohol	8—10	100	93
	Dioxane	15—20	90	80
	Water	15—20	96	66

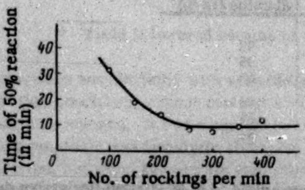


Fig. 1. Relation of rate of reduction of a mixture of hexamethylenediamine–acetone to conditions of mixing.

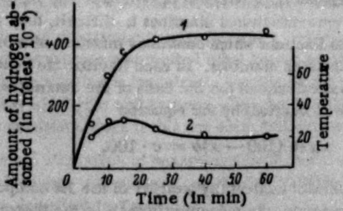


Fig. 2. Change in temperature during reduction of a mixture of hexamethylenediamine–butyraldehyde. 1) Amount of hydrogen absorbed, 2) temperature.

The best solvent was ethyl alcohol. The use of water is limited not only by the fact that it does not dissolve a large number of carbonyl compounds, but also because the products of alkylation of hexamethylenediamine are solid, water-insoluble hydrates. The formation of a solid phase makes hydrogenation difficult and shifts the reaction toward formation of monosubstitution products.

Effect of mixing. For a determination of the reaction kinetics we carried out experiments with a different amount of rocking the ampules (alkylation compound, acetone; initial pressure 110 atmos). As Fig. 1 shows, under the conditions which we used,the shortest time is reached at 250 rockings per min. In all further experiments we used 280-300 rockings per min.

Effect of temperature. Reductive alkylation of hexamethylenediamine goes exothermally (Fig. 2) with sufficient speed and to the end at room temperature. Increasing the temperature (120-130°) is advisable when alkylating with highly branched ketones (diisobutyl ketone) since at lower temperatures these almost do not react, as Fig. 3 shows.

Effect of catalyst. For this reaction we used the ordinary hydrogenation catalysts. The results are shown in Table 2.

Effect of concentration and ratio of reagents. The concentration of diamine and alkylating agent under the experimental conditions does not affect the reaction rate within definite limits (~ 30%). Further increase in concentration leads to decreased yield of N,N'-dialkylation products due to partial tarring and increase in high-boiling fractions (Table 3).

The ratio of reaction components has the following effects. With insufficient alkylating agent we get a mixture of N-mono- and N,N'-disubstituted diamine. With the theoretical ratio of components almost no monosubstituted diamine is obtained. An excess of alkylating agent in the case of use of acetaldehyde or propion-

TABLE 2

Relation of Reductive Alkylation Reaction of Hexamethylenediamine by Acetone to Nature of Catalyst

Catalyst	Weight of catalyst calculated as metal (in g)	Time of occurrence of 50% reaction (in min)	Extent of reaction (in %)	Yield of N,N'-dialkyl derivative based on starting diamine (in %)
Platinum black	0.185	8—10	100	93—96
Palladium on $BaSO_4$	0.200	25—30	90	75—80
Raney nickel	3.000	120	86	70

TABLE 3

Effect of Concentration of Reagents on Rate of Hydrogen Absorption and Yield of N,N'-Dialkylated Products

Alkylating compound	Conc. on diamine (in M)	Absorption of H_2 in 20 min (in mmole)	Extent of reaction (in %)	Yield of N,N'-dialkyl derivative based on starting diamine (in %)
Acetone	1.0	161	100	93
	2.0	165	100	95
	3.7	115	79	68
Butyraldehyde	1.0	77	100	84
	2.0	77	100	85
	3.4	43	72	54

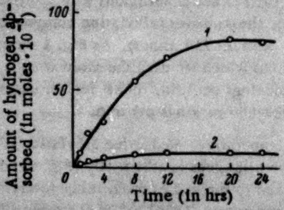


Fig. 3. Rate of reduction of a mixture of hexamethylenediamine—diisobutyl ketone at different temperatures. 1) at 130°, 2) at 20°.

aldehyde causes a lowered yield of N,N'-dialkyl derivative due to formation of products of a greater degree of alkylation. In the case of use of ketones and higher aldehydes their excess did not affect the yield of the chief reaction products (under the conditions described).

Since the separation of mixtures of N-mono- and N,N'-dialkyl and also tri- and tetra-substituted diamines is difficult, they were separated only into fractions which contained mixtures of mono-, di-, or tri- and tetraalkylated diamines. In each fraction the content of the components was calculated (on the basis of the determined total nitrogen in the given fraction) by the equation

$$xa + (100 - x)b = c \cdot 100,$$

where: x is the percent content (by weight) of the 1st component in the mixture (for example, the monosubstituted), a the theoretical percent content of N in the 1st component, b the theoretical percent content of nitrogen in the 2nd component (disubstituted diamine), c the percent content N in the fraction, found by analysis.

The resulting data are given in Table 4. With excess acetaldehyde and propionaldehyde we found an increased amount of tri- and tetrasubstituted diamines. When we used ketones and aldehydes with a C_4 chain no effect of excess alkylating compound was observed. This effect is evidently explained by the increasing steric effects of the substituting groups because of the increasing length and branching of the chains. Such groups hinder further alkylation of the amino groups to tertiary amines.

Effect of structure of alkylating compound. The above optimum conditions for carrying out the reaction when alkylating with acetone and butyraldehyde were also used in the main with other carbonyl compounds. The only changes were in temperature regime and method of isolating the reaction products.

TABLE 4

Effect of Ratio of Reagents on Yield of N,N'-Dialkyl Hexamethylenediamines (based on taken diamine)

Alkylating compound	Molecular ratio of hexamethylenediamine and carbonyl compound	Yield		
		N-monoalkyl derivative (in %)	N,N'-dialkyl derivative (in %)	mixture of tri- and tetraderivatives (in %)
Acetone	1 : 1	15	34	none
	1 : 2	none	93	none
	1 : 3	none	90	none
Butyraldehyde	1 : 1	20	32	none
	1 : 2	none	86	none
	1 : 3	none	82	none
Propionaldehyde	1 : 1	18	36 *	none
	1 : 2	none	58 *	27
	1 : 3	none	37	52
Acetaldehyde	1 : 1	21	32 *	none
	1 : 2	—	41 *	13
	1 : 3	none	19	69

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* Yield is lowered because of formation of unsymmetrical N-dialkyldiamine.

Thus, when we alkylated with acetaldehyde, in order to avoid tarring of the latter (which occurs intensively under reaction conditions without cooling) we cooled to −8 to −10° in the initial period of the reaction (when mixing the components). It was advisable to add the aldehyde to the diamine solution in a hydrogen atmosphere. When using propionic and isobutyric aldehydes we also recommend cooling (from 0 to −3°) in the initial period of the reaction, but when ketones are used this is not necessary. The use of higher temperatures in the alkylation of diisobutyl ketone has already been mentioned.

Isolation of the reaction products usually consists of the following steps: 1) distillation of the volatile products from the reaction mixture (solvent and excess carbonyl compound), 2) washing the ether solution with water to remove unreacted hexamethylenediamine, 3) drying the mixture after washing, 4) distillation in a vacuum (in an atmosphere of nitrogen) to remove the N,N'-dialkylation products.

The step of washing out the hexamethylenediamine can often be omitted, as for example in the case of alkylation by acetone and methyl ethyl ketone where reaction goes almost to completion. In the case of using acetaldehyde, washing is inadvisable because of the appreciable solubility in water of the dialkylation product. With higher aldehydes and ketones, when the alkylation reaction does not go to completion, washing out the diamine is necessary, since if this not done, isolation of a pure product by distillation is very difficult.

For the alkylation of hexamethylenediamine we used acetaldehyde, propionaldehyde, n-butyraldehyde, isobutyraldehyde; and acetone, methylethyl ketone, and diisobutyl ketone. We obtained a series of compounds which are described in Table 5.

EXPERIMENTAL

The experiments were carried out in a steel autoclave with a heater, capacity 150-200 ml, which was set in a shaking apparatus. The course of the reaction was controlled by the fall in pressure. The reaction mixture was analyzed for total nitrogen content, primary amines, and carbonyl groups. Separation of the reaction products was carried out by fractional distillation in a vacuum.

Alkylation with n-butyraldehyde. In the autoclave we placed a solution of 23.2 g of hexamethylenediamine in 50 ml of 96% alcohol, and then with ice cooling we added 28.8 g of n-butyraldehyde and 0.2 g of platinum oxide (prepared according to Adams). The autoclave was closed, and hydrogen was twice passed in under pressure to 50 atoms, then it was filled with hydrogen to a pressure of 150 atmos, and the apparatus was placed on the shaker at room temperature. Absorption of hydrogen was followed for 60 min to a final pressure

TABLE 5

N,N'-Dialkyl Derivatives of Hexamethylenediamine

Name of compound and its formula	Boiling point (pressure in mm)	d_4^{25}	n_D^{25}	Yield		Analytical data (in %)						MR_D	
						N (total)		NH *		found (by molecular wt.			
				on starting diamine	on reacting diamine	found (Kjehldahl)	calc.	found (by acetylation)	calc.	found (Rast)	calc.	found	calculated
N,N'-Diethylhexamethylenediamine	101—105° (7)	0.825	1.4440	41	47	16.2	16.3	16.3	16.3	168	172	55.4	55.6
N,N'-Di-n-propylhexamethylenediamine	102—105 (2)	0.831	1.4451	58	64	14.0	14.0	13.9	14.0	196	200	64.2	64.8
N,N'-Diisopropylhexamethylenediamine**	110—112 (3)	0.816	1.4393	95	95	14.1	14.0	13.9	14.0	201	200	64.8	64.8
N,N'-Di-n-butylhexamethylenediamine	131—133 (3)	0.825	1.4479	87	90	12.2	12.3	12.4	12.3	238	228	73.9	74.1
N,N'-Diisobutylhexamethylenediamine	112—115 (2)	0.818	1.4481	85	86	12.5	12.3	—	—	220	228	74.0	74.1
N,N'-Dibutyl-2-hexamethylenediamine**	115—118 (2)	0.828	1.4475	90	90	12.5	12.3	—	—	232	228	73.5	74.1
N,N'-Di-(2,6-dimethylheptyl-4)-hexamethylenediamine**	183—184 (2)	0.835	1.4554	25	66	7.7	7.6	—	—	354	368	119.7	120.2

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* The NH_2 group determined according to Van Slyke was absent in all the compounds.

** Obtained first.

of 30 atmos which corresponded to an absorption of 400 mmoles of H_2 (100%). After discharge of pressure and settling of the catalyst, the reaction mixture was analyzed for content of primary amino groups by the Van Slyke method, showing 2.4% NH_2-groups (of the starting amount). The alcohol was distilled from the reaction mixture, the residue was dissolved in 200 ml of ether, the unreacted diamine was washed out with 150 ml of water (in 25 ml portions) and was dried over K_2CO_3. After distilling off the ether the alkylation product was separated by distillation in a vacuum (in an atmosphere of nitrogen) from a flask with a rectifying column. Almost all the product came over at 128-132° (2-3 mm) and was obtained in the amount of 39.5 g (yield 87% on amount of diamine in the reaction). The analytical data for the resulting N,N'-di-n-butylhexamethylenediamine are given in Table 5.

Alkylation with acetone was carried out under the same conditions. To a solution of 23.2 g of hexamethylenediamine in 50 ml of alcohol was added (without cooling) 23.2 g of acetone and 0.2 g of catalyst. The fall in hydrogen pressure was from 150 to 30 atmos which corresponded to an absorption of 403 mmoles H_2 (101%) over 35 min. There were no primary amino groups in the mixture; therefore the mixture was distilled without washing after drying. Almost all the product passed over at 102-104° (2 mm) and was obtained in the amount of 38.3 g (yield 96%). The analytical data for the resulting compound are given in Table 5.

To confirm the structure of the resulting N,N'-diisopropylhexamethylenediamine we took its infrared spectrum* from 2 to 10 μ. In the spectrum we found bands at 3292 cm^{-1} which belonged to the N−H oscillation. At 1400-1800 cm^{-1} there was no absorption which showed the absence of the groups C=O, C=N, C=C, and NH_2 in the compound studied.

SUMMARY

1. On the basis of the reductive alkylation reaction we worked out a method for the synthesis of N,N'-dialkyl derivatives of hexamethylenediamine with various substituents, which assures a series of alkyl compounds in high yield.

2. The optimal conditions for the reaction are: ethyl alcohol as solvent, reagent concentration of 20-25% (of the diamine); ratio of diamine to carbonyl compound (in moles) 1 : 2; platinum black catalyst (0.1-0.05%); reaction temperature 20-25° (except in special cases); hydrogen pressure during the reaction 120-150 atmos.

3. We have studied and characterized seven N,N'-dialkyl derivatives of hexamethylenediamine, three of them synthesized for the first time.

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Received April 11, 1957

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* The spectroscopic study was made by L. D. Shcherb.

** Russian translation.

RESEARCH IN THE FIELD OF SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

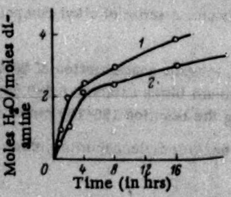
II. THE SYNTHESIS OF N-MONOALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

The preparation of N-monosubstituted derivatives of hexamethylenediamine under conditions which preserve the special features of reduction alkylation [1], involves many difficulties. Reaction of the carbonyl compounds with the NH_2 group of either the free or monosubstituted diamine (present in solution) is equally probable, at least in the early stages of the reaction. This leads to the formation of a mixture of N-mono- and N,N'-dialkyl diamines that is difficult to separate and contains a considerable proportion of the disubstituted component, which lowers the yield of N-monoalkyl diamine correspondingly.

In order to direct the reaction towards the N-monosubstituent side, use was made of an observation made by us concerning the formation of solid, water-insoluble hydrates of both N-mono- and N,N'-dialkylated diamines.

It was established that in order to direct the reaction preferentially towards the N-monoalkylation side it should be carried out in an aqueous medium and the ratio of alkylating agent to diamine should be decreased (to 1 mole per mole of diamine). The increase in yield of monosubstituted diamine is fostered by the fact that in an aqueous medium it precipitates as a solid phase (in the form of the hydrate). This reduces the probability of the second amino group reacting with the alkylating agent and ensures that the reaction is directed mainly towards mono-alkylation.



Variation of molar quantity of H_2O combined with substituted diamines, with time. 1) N,N'-di-n-butylhexamethylenediamine, 2) N,N'-diisopropylhexamethylenediamine.

The formation of hydrates was studied quantitatively from the example of disubstituted derivatives, namely N,N'-di-n-butyl- and N,N'-diisopropylhexamethylenediamine. Di-substituted diamines on addition of water, in an atmosphere saturated with water vapor, or on standing over water form, solid, crystalline, white hydrates. On placing these in a desiccator over P_2O_5 the water splits off completely and the residual diamine, by refractive index and nitrogen content, is identical with that first taken.

As is seen from the graph,* 1 mole of substituted diamine rapidly combines with 2 moles of H_2O to form the hydrate.** Further combination with water takes place much more slowly. Under the experimental conditions the maximum combination of water achieved was 4 moles per 1 mole of diamine. The dihydrate of N,N'-di-n-butylhexamethylenediamine is insoluble in water; the dihydrate of N,N'-diisopropylhexamethylenediamine dissolves in a large proportion of water. N,N'-diisobutyl-, N,N'-di-n-butyl-2-hexamethylenediamine, etc. also form hydrates.

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* The data presented were calculated from the increase in weight of the diamine resulting from the addition of water in a desiccator over H_2O.

** Analysis of N,N'-di-n-butylhexamethylenediamine dihydrate. Found %: N (titrated) 10.5. M 280. $C_{14}H_{36}N_2O_2$. Calculated %: N 10.3. M 264.

Monosubstituted diamines (N-n-butyl- and N-isopropylhexamethylenediamine) also form crystalline hydrates in air (in an atmosphere saturated with H_2O vapor). For the monosubstituted diamines this fact was established qualitatively but was not studied quantitatively.

The formation of hydrates evidently explains the lowering of the yield of N,N'-dialkyl diamine and the formation of some quantity of N-monosubstituted diamine on carrying out the reduction alkylation reaction in water [1].

The method for preparing the monosubstituted derivative was worked out by us for N-mono-n-butylhexamethylenediamine but it can be used for the synthesis of other monosubstituted derivatives that form hydrates that are insoluble or difficultly soluble in water. N-monoisopropylhexamethylenediamine hydrate is soluble in a large proportion of water; however, even in this case carrying out the reaction in an aqueous medium increases the yield of the N-monosubstituted diamine. The results obtained are given in Table 1.

TABLE 1

Yield of N-Monoalkylhexamethylenediamine on Reduction Alkylation in Alcohol and in an Aqueous Medium

N-monosubstituted diamine	Whether hydrate is insoluble in water	Yield (in %) calculated on diamine taken	
		in alcohol	in water
N-Mono-n-butylhexamethylenediamine	+	20	65
N-Monoisopropylhexamethylenediamine	−	15	43

EXPERIMENTAL

Alkylation with n-butyraldehyde. A solution of 13.45 g hexamethylenediamine in 20 ml water was placed in an autoclave (volume 150-200 ml) and 8.3 g n-butyraldehyde and 0.2 g platinum oxide were added. The autoclave was closed, swept out with hydrogen and filled with hydrogen to 103 atmos and (at room temperature) placed on a shaker. Absorption of hydrogen was observed for a period of 40 min, the final pressure was 72 atmos corresponding to the absorption of 230 mmoles H_2 (100%). After completion of hydrogenation the crystals of the hydrate of the alkylated diamine were washed with 50 ml water on a vacuum filter. They were then dissolved in 100 ml ether, the solution dried with K_2CO_3 and after removal of catalyst and evaporation of the ether the residue was distilled in a current of nitrogen. The vapor temperature rose immediately to 101-102° (3 mm) and the first fraction corresponding to the N-monoalkyl derivative distilled within these limits. A jump in temperature to 130° (3 mm) was then observed, corresponding to distillation of the disubstituted derivative. There was little still residue. The yield of N-mono-n-butylhexamethylenediamine was 13.0 g (65% calculated on the diamine charge or 80% calculated on the diamine reacted). Analytical data are given in Table 2.

TABLE 2

Analysis of N-Monoalkyl Derivatives of Hexamethylenediamine

Substance	Boiling point (pressure in mm)	d_4^{25}	n_D^{25}	Analytical data (%)				Found Molecular wt.		MR_D	
				N (total)		N (amino)					
				found (Kjeldahl)	calc.	found (Van Slyke)	calc.	found	calc.	found	calc.
N-Mono-n-butylhexamethylenediamine	101—102° (3)	0.833	1.4550	16.2	16.3	8.10	8.15	174	172	55.5	55.4
N-Monoisopropylhexamethylenediamine	87—87.5 (2)	0.830	1.4465	17.5	17.7	8.50	8.75	159	158	50.8	50.8

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* Prepared and characterized for the first time.

Alkylation with acetone. 6.1 g acetone and 0.5 g platinum oxide were added to a solution of 12.2 g hexamethylenediamine in 25 ml water. A fall in hydrogen pressure from 107 to 79 atmos over a period of 30 min was observed, corresponding to 204 mmoles of absorbed hydrogen (97%). After completion of hydrogenation and settling of the catalyst the reaction mixture consisted of a homogeneous solution. In order to isolate the alkylation products the aqueous solution was extracted several times with ether. The ethereal layer was dried and the ether distilled off. On distilling the reaction products the vapor temperature rose immediately to 87-87.5° (2 mm) and the first fraction corresponding to the N-monoalkyl derivative was taken off within these limits. The temperature then rose to 104-106° (2 mm) at which temperature the second fraction was distilled off. The yield of N-monoisopropylhexamethylenediamine was 7.2 g (43% calculated on the diamine charge or 61% calculated on the diamine reacted). The analytical data are given in Table 2.

SUMMARY

1. A method has been developed for the synthesis of N-monoalkyl derivatives of hexamethylenediamine by reduction alkylation in an aqueous medium, characterized in that the product of monoalkylation separates in the hydrate form, which precipitates (for a number of carbonyl compounds) as a solid phase.

2. It has been established that also in cases where soluble hydrates are formed the use of water as solvent increases the yield of hexamethylenediamine N-monoalkyl derivatives.

3. Two hexamethylenediamine N-monoalkyl derivatives have been studied and characterized, N-monoisopropylhexamethylenediamine being synthesized for the first time.

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Received April 11, 1957

SYNTHESIS OF ALKOXY-SUBSTITUTED KETONES OF THE ISOQUINOLINE SERIES

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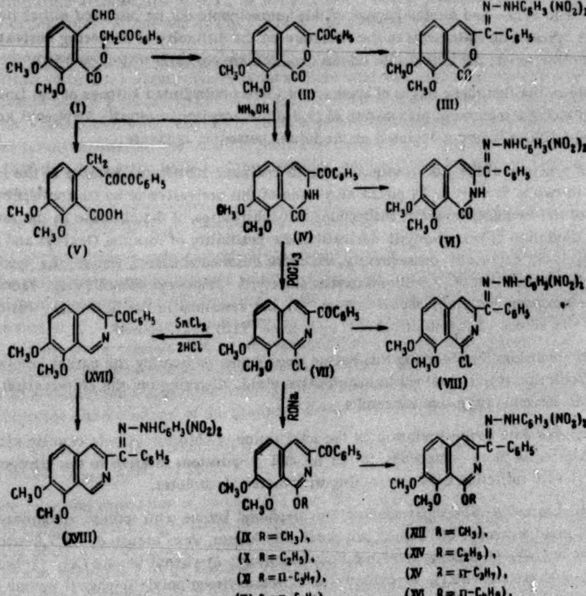
A large number of substances possessing high physiological activity and used in medicine are encountered among the isoquinoline compounds. A little studied group of isoquinoline compounds are the ketones of this series – substances which up to the present time are not readily available.

The problem of the present work consisted in the development of methods of preparation of a number of alkoxy-substituted ketones of the isoquinoline group from the available opianic (5,6-dimethoxy-o-aldehydobenzoic) acid, which occurs as a by-product in the production of the opium alkaloids. The ketones, the synthesis of which was developed, are close in structure to papaverine and papaveraldine – substances possessing spasmolytic activity. We achieved the synthesis of these ketones in a few stages as shown in the scheme below. (The thick arrows indicate the course of the main reaction.)


(I)
(II)
(III)
NH_4OH
(IV)
(V)
(VI)
$POCl_3$
$SnCl_2$
$2HCl$
(VII)
(VIII)
(XVII)
RONa
(XVIII)
(IX R = CH₃),
(X R = C₂H₅),
(XI R = n-C₃H₇),
(XII R = n-C₄H₉).
(XIII R = CH₃),
(XIV R = C₂H₅),
(XV R = n-C₃H₇),
(XVI R = n-C₄H₉).

The preparation of the α-ester of opianic acid and ω-hydroxy acetophenone (I) from potassium opianate, and the preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II) as a result of intramolecular condensation of this α-ester in the presence of piperidine has been reported earlier [1]. Further study of the conditions of intramolecular condensation of the above α-ester showed that on substitution of piperidine by diethylamine the yield is improved (60%). It was further shown that intramolecular condensation takes place also in the absence of a basic catalyst: on distilling the benzene from the filtrates obtained during crystallization of the α-ester the mixture was overheated; in this case not the original α-ester but (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II), was found in the residue. This ketone was also obtained in high yield (90%) on distilling benzene from the pure α-ester on a sand bath. In the absence of benzene the ketone (II) is obtained from the α-ester only after more prolonged heating in vacuo at a higher temperature, considerable resinification occurring under these conditions. The ease with which the reaction proceeds on distilling off benzene is evidently explained by the fact that the benzene carries away the water formed in the condensation.

In order to characterize the ketone obtained, its 2,4-dinitrophenyl hydrazone (III) was prepared successfully. As has already been reported [1] this ketone does not react with a number of other carbonyl group reagents (hydroxylamine, semicarbazide) under the usual conditions.

Ketone (II) reacts with ammonia in acetic acid solution [1] forming (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (IV). Further study of the amidation reaction, in particular amidation in an aqueous medium, showed that on heating a ketone of the isocoumarin series with aqueous ammonia hydrolysis of the isocoumaryl ring and formation of the diketo acid (V), previously described in the literature [2], takes place. This is the cause of the low (50%) yield of amidation product. In order to avoid hydrolysis of the starting material an attempt was made to carry out the reaction with aqueous ammonia in the cold. Amidation proceeds so slowly in the cold that it was practically impossible to detect any amidation product in the reaction mixture after 2-3 days and its quantitative formation was observed only after allowing the mixture to stand for 6 months.

For characterization of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (IV) its 2,4-dinitrophenyl hydrazone (VI) was prepared. The oxime and semicarbazone of this ketone could not be prepared either in alcohol or pyridine solution. This agrees with statements in the literature on the difficulty of preparing derivatives of some ketones of the isoquinoline series, the hetrocyclic nuclei of which are partially hydrolyzed [3].

Thus the study of the first three stages of synthesis of alkoxy-substituted ketones of the isoquinoline series led to the development of a method of preparation of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (IV) with a total yield of about 80% of theory calculated on the initial potassium opianate.

Conversion of a ketone of the isocarbostyril series to 1-alkoxy-substituted ketones of the isoquinoline series could be achieved in two ways — either by direct alkylation of this derivative or by its conversion of a 1-chloro-substituted ketone of the isoquinoline series with subsequent substitution of the chlorine in the latter by alkoxy groups. On direct alkylation of isocarbostyril derivatives the possibility of forming O-alkyl and N-alkyl derivatives simultaneously is not excluded; consequently, we chose the second route. Hence, the next stage in the synthesis consisted in chlorination of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (VII). From this reaction (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (VI), not described in the literature, was obtained. For characterization of the ketone its 2,4-dinitrophenyl hydrazone (VIII) was prepared.

The optimum conditions for obtaining this ketone were found: on heating the parent ketone for a short time with phosphorus oxychloride it was obtained in quantitative yield. Carrying out the chlorination under other conditions (PCl_5, organic solvents) gave inferior results.

From the extensive data in the literature on the substitution of chlorine in heterocyclic nitrogen compounds, it is evident that chlorine in these compounds, in the α- and γ-positions relative to the nitrogen, generally exchanges with alkoxyl with sufficient ease on reacting with metal alcoholates.

On heating (1-chloro-7,8-dimethoxyisoquinoline-3)-phenyl ketone with sodium alcoholates in solution in the corresponding alcohol, a number of ketones, not previously known, were prepared: (1,7,8-trimethoxyisoquinolyl-3)-phenyl ketone (IX), (1-ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (X), (1-propoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XI), (1-butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XII). The ketones were characterized by the 2,4-dinitrophenyl hydrazones (XIII-XVI).

In order to prepare a ketone of the isoquinoline series not containing an alkoxy group in position 1 in the isoquinoline nucleus, the 1-chloro-substituted isoquinoline ketone that we prepared was reduced. By using stannous chloride and hydrochloric acid as reducing agent (7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XVII), not previously known, was obtained. This ketone was characterized by the 2,4-dinitrophenyl hydrazone (XVIII).

EXPERIMENTAL

Preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II). a) 3.28 g of the α-ester of opianic acid and ω-hydroxyacetophenone (I) were placed in a round-bottomed flask fitted with a reflux condenser and moistened with 10 drops of diethylamine. The mixture was heated on a boiling water bath. After heating for 16 hrs 10 ml ethyl alcohol and 10 ml toluene were added to the contents of the flask and heating was continued for a further 10-15 min. The mixture was then cooled and the crystals were filtered off and washed with alcohol. The crude product melted at 169-170°; after recrystallizing from ethyl alcohol m. p. 172°. According to the literature it has m. p. 172°. Yield 1.86 g, i. e., about 60%.

b) 3.28 g of the α-ester (I) and 10 ml benzene were placed in a round-bottomed flask fitted with a downward condenser and a thermometer reaching almost to the bottom of the flask. The benzene was distilled off from a sand bath; during this process the temperature of the mixture reached 160-170° and this temperature was maintained for 15-20 min. To the residue, consisting of a viscous, light-yellow liquid, 10 ml alcohol and 10 ml toluene were added. The mixture was cooled and the crystalline product was filtered off and washed with alcohol. M. p. 168°; after recrystallizing from alcohol and from toluene it remained unchanged. A test sample of the product mixed with (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (m. p. 172°) melted at 170°. Yield 2.78 g (about 90%).

c) 3.28 g of the α-ester (I) was heated at 250-300° for 2 hrs in a round-bottomed flask connected to a vacuum pump. The reaction product was treated as in experiment "a". The crude product had m. p. 166-168°; after recrystallizing from alcohol, m. p. 168°. A sample mixed with (7,8-dimethoxyisocoumaryl-3)-phenyl ketone prepared in experiment "a" melted at 170°. Yield 1.91 g (about 70%).

(7,8-Dimethoxyisocoumaryl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (III). 0.5 g of 2,4-dinitrophenyl hydrazine was dissolved in 1 ml warm, concentrated sulfuric acid and 5 ml ethyl alcohol was added to the solution. Then a solution of 0.3 g ketone (II) in 50 ml ethyl alcohol was added immediately to the dinitrophenyl hydrazine solution. The 2,4-dinitrophenyl hydrazones obtained from preparations of ketone (II) formed under various conditions (experiments "a," "b" and "c") and also from the mixed test samples melted at the same temperature (m. p. 256° in a Maquenne block). Crystallization was carried out from a mixture of equal parts of alcohol and ethyl acetate.

Found %: N 11.60. $C_{24}H_{18}O_8N_4$. Calculated %: N 11.42.

Preparation of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (IV). a) A mixture of 1.0 g ketone (II) and 100 ml of a 25% aqueous solution of ammonia was boiled for 3 hrs in a round-bottomed flask with a reflux condenser connected to a mercury trap. The mixture was then cooled and filtered and the residue washed with water. The residue consisted of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone. Yield 0.5 g (about 50%). M. p. 199° (from alcohol). Almost white crystals with a faint yellowish-green tinge. This substance was practically insoluble in water; readily soluble in dichloroethane, chloroform, pyridine and glacial acetic acid; slightly soluble in cold alcohol, soluble to a considerable extent on heating. Alcoholic solutions of ketone (IV) did not give the coloration with ferric chloride characteristic of the majority of isocarbostyril derivatives.

Found %: C 69.86; H 5.06; CH_3O 20.67; $H_{act.}$ 1.02. M 298. $C_{18}H_{15}O_4N$. Calculated %: C 69.89; H 4.89; $2CH_3O$ 20.07; $H_{act.}$ 1.00. M 309.

The filtrate from the separation of ketone (IV) from the reaction mixture was acidified with 10% sulfuric acid until acid to Congo. This brought about the separation of an acid which was filtered off and washed with water. Its melting point was 120-130° (decomp.). From its properties this acid was identical with the diketo acid obtained by Bain and co-workers [2] by alkaline hydroxlysis of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone. Yield 0.4 g (about 40%). For purification the acid was twice reprecipitated by water from solution in methyl alcohol. M. p. 128-130° (decomp.); according to the literature, m. p. about 130° (decomp.).

Found: neutralization equiv. 324. $C_{18}H_{16}O_6$. Calculated: neutralization equiv. 328.

b) A mixture of 0.5 g of finely powdered ketone (II) and 25 ml of 25% aqueous ammonia was allowed to stand at 8-10°. A sample of the solid material taken after 5 days had m. p. 172°; nitrogen could not be detected in the sample. No precipitate was obtained on acidifying the filtrate with sulfuric acid. The reaction mixture was left in a refrigerator and after 6 months the solid material was filtered off and washed with water. M. p. 199°. A mixed sample with ketone (IV) obtained previously [1] and in experiment "a" had m. p. 199°. Yield 0.45 g (quantitative, allowing for test sample removed). The filtrate obtained after separation of the solid product from the reaction mixture did not contain the diketo acid (V).

(7,8-Dimethoxyisocarbostyril-3)-phenyl ketone 2,4-dinitrophenylhydrazone (VI) was prepared by the method described above.

Found %: N 14.17. $C_{24}H_{19}O_7N_5$. Calculated %: N 14.31.

The 2,4-dinitrophenylhydrazone (VI) crystallized from glacial acetic acid with 1 molecule of acetic acid.

Preparation of (1-chloro-7,8-dimethoxyisoquinoline-3)-phenyl ketone (VII). 3.1 g of ketone (IV) and 3 ml (excess) phosphorus oxychloride were placed in a round-bottomed flask fitted with a reflux condenser and a calcium chloride drying tube. The mixture was heated on a boiling water bath for 20 min, then after cooling, poured onto ice. The product, which crystallized out rapidly, was filtered off and washed with water. The yield of ketone (VII) was 3.1 g (99%) with m. p. 144° (from benzene or ethyl alcohol). Ketone (VII) was a colorless, crystalline substance. It was practically insoluble in water but soluble in organic solvents.

Found %: C 66.08; H 4.48; N 4.30; Cl 10.80. $C_{18}H_{14}O_3NCl$. Calculated %: C 65.96; H 4.31; N 4.27; Cl 10.82.

(1-Chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (VIII) was prepared by the method described above. The orange crystals of the dinitrophenylhydrazone were filtered off after 10 min (to avoid hydrolysis with splitting off of chlorine in the acidic medium). M. p. (in a Maquenne block) 236-242° (from nitrobenzene).

Found %: 13.87. $C_{24}H_{18}O_6N_5Cl$. Calculated %: N 13.79.

Preparation of the (1-alkoxy-7,8-dimethoxyisoquinoline-3)-phenyl ketones (IX-XII). To a solution of 3.28 g of ketone (VII) in 150 ml of the alcohol (methyl, ethyl, propyl, butyl) a solution of the sodium alcoholate, prepared from 0.25 g sodium and 10 ml of the same alcohol, was added. The mixture was heated on the water bath at 60-70° for 16 hrs, the reflux condenser being connected to a calcium chloride tube. The sodium methylate, ethylate and propylate reaction products were isolated by pouring the reaction mixtures into 300 g ice-water. The product which separated was filtered off, washed with water to neutral reaction to phenolphthalein and recrystallized from ethyl alcohol. To isolate the sodium butylate reaction product the mixture was washed with water to neutral reaction to phenolphthalein, the solution of the ketone in butyl alcohol dried over sodium sulfate and the alcohol distilled off in vacuo.

a) (1,7,8-Trimethoxyisoquinolyl-3)-phenyl ketone (IX). Yield 2.74 g (85%); m. p. 134°.

Found %: C 70.65; H 5.43; N 4.39. $C_{19}H_{17}O_4N$. Calculated %: C 70.58; H 5.30; N 4.33.

b) (1-Ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (X). Yield 2.66 g (79%); m. p. 120°.

Found %: C 71.16; H 5.85; N 4.15. $C_{20}H_{19}O_4N$. Calculated %: C 71.20; H 5.68; N 4.15.

c) (1-Propoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XI). Yield 2.88 g (82%); m. p. 78°.

Found %: C 71.81; H 6.02; N 4.02. $C_{21}H_{21}O_4N$. Calculated %: C 72.31; H 6.34; N 3.83.

d) (1-Butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XII). Yield 3.06 g (84%); m. p. 91-92° (from alcohol.

Found %: C 72.42; H 6.27; N 3.97. $C_{22}H_{23}O_4N$. Calculated %: C 72.31; H 6.34; N 3.83.

The ketones obtained were crystalline solids, practically insoluble in water, soluble in organic solvents. On passing dry hydrogen chloride through ethereal solutions of the ketones the corresponding salts, which are readily hydrolyzed by water, separated out.

The 2,4-dinitrophenylhydrazones of these ketones were prepared by the method described above. These derivatives were recrystallized from a mixture of equal volumes of alcohol and ethyl acetate.

a) (1,7,8-Trimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XIII). M. p. 174-175°.

Found %: N 14.16. $C_{25}H_{21}O_7N_5$. Calculated %: N 13.91.

b) (1-Ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XIV). M. p. 210°.

Found %: N 13.64. $C_{26}H_{23}O_7N_5$. Calculated %: N 13.50.

c) (1-Propoxy-7,8-dimethoxyisoquinonyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XV). M. p. 178°

Found %: N 13.28. $C_{27}H_{25}O_7N_5$. Calculated %: N 13.19.

d) (1-Butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XVI). M. p. 137-138°.

Found %: N 12.49. $C_{28}H_{27}O_7N_5$. Calculated %: N 12.84.

Preparation of (7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XVII). A mixture of 3.28 g (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (VII), 2.48 g of finely powdered $SnCl_2 \cdot 2H_2O$ and 12 ml conc. HCl (d 1.18) was heated on a wire gauze under reflux for half an hour. The solid material rapidly dissolved and after 15-20 min a crystalline product began to separate. Heating was continued for a further 3 hrs (on a boiling water bath) after which the reaction mixture was cooled to room temperature and the crystals filtered off and washed with concentrated hydrochloric acid. The crystalline product was heated with 50 ml 10% KOH for half an hour, after which the mixture was cooled and filtered. The solid product was washed with KOH solution and water, dried and extracted with ether. The ether was distilled from the ethereal extract and the residue, consisting of ketone (XVII), was recrystallized from petroleum ether and from alcohol. Yield 1.03 g (35%).

M. p. 104°. This material was slightly soluble in water, readily soluble in ether and the majority of organic solvents.

Found %: C 73.71; H 5.20; N 4.72. $C_{18}H_{15}O_3N$. Calculated %: C 73.71; H 5.16; N 4.77.

The residue after extraction of ketone (XVII) with ether was extracted several times with hot chloroform. The residue (1.4 g) after removal of chloroform was a crystalline substance with m. p. 238° (from nitrobenzene), practically insoluble in water and in ether; in the majority of organic solvents it was only slightly soluble in the cold.

(7,8-Dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XVIII) was prepared by the method described above. M. p. 268° (from nitrobenzene in a Maquenne block).

Found %: N 12.04. $C_{24}H_{13}O_6N_5 \cdot H_2SO_4$. Calculated %: N 12.25.

SUMMARY

A method has been developed for the preparation from opianic acid of a number of alkoxy-substituted ketones of the isoquinoline group. The preparation of these ketones was accomplished in a few stages as follows:

1. Intramolecular condensation of the α-ester of opianic acid and ω-hydroxyacetophenone. It was shown that this reaction takes place both with and without organic bases. Conditions have been found for the preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone in high yield (90%).

2. Amidation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone. It was shown that amidation in glacial acetic acid proceeds more satisfactorily than in aqueous solution.

3. Chlorination of (7,8-dimethoxyisocarbostyril -3)-phenyl ketone. Conditions were found whereby (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone could be prepared in quantitative yield.

4. a) Reaction of (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone with sodium alcoholates whereby a number of (1-alkoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketones were obtained, with different alkoxy groups (OCH_3, OC_2H_5, OC_3H_7, OC_4H_9) in position 1.

b) Reduction of (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone with stannous chloride and hydrochloric acid, giving (7,8-dimethoxyisoquinolyl-3)-phenyl ketone.

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Received March 18, 1957

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[*] Original Russian pagination. See C. B. translation.

THE ACTION OF NITROUS ACID ON CYCLIC SALTS OF SALICYLIC ACID. THE PREPARATION OF 5-DIAZOSALICYLIC ACID

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V. M. Rodionov and V. K. Matveev [1] have shown that 5-diazo-2-phenolsulfonic acid and 3-diazo-4-phenolsulfonic acid are formed readily by the action of nitrous acid on o- and p-phenolsulfonic acids. The formation of the diazo compounds in this way proceeds through the stage of the corresponding nitroso compounds which by reacting further with oxides of nitrogen and nitrous acids are converted to the diazonium nitrates [2, 3].

In the case of salicylic acid the preparation of the corresponding nitroso compound by the action of nitrous acid has not so far been successful. Salicylic acid is evidently not sufficiently reactive for this. Papers describing the preparation of nitrososalicylic acid by the action of nitrous acid [4, 5] were shown to be in error [6]. Salicylic acid in this case reacts with nitrous acid with evolution of CO_2 and the formation of o-diazophenol. o-Nitrosophenol is formed as an intermediate product.

Study of the reactivity of cyclic salts of salicylic acid with respect to azo coupling indicates that some of these have a considerably increased reactivity in this reaction, in comparison with free salicylic acid. Cyclic aluminum, chromium, zinc and beryllium salicylates were shown to be particularly active under conditions where intramolecular dissociation [7], which for the cyclic salicylates mentioned takes place in acidic media, occurred to a sufficient extent. For this reason the cyclic salicylates in acid media have the same activity as that of alkaline solutions of salicylic acid having the same degree of dissociation of the phenolic hydroxyl.

Since the azo coupling reaction of phenols and naphthols is very similar to the nitrosation reaction [8, 9] an increase in the activity of the above-mentioned cyclic salicylates in the nitrosation reaction, might also be expected. In confirmation of this assumption it was established that the cyclic salicylates have a high reactivity in the reaction in question and react with nitrous acid with the addition of a nitroso group in the para position relative to the hydroxyl. The carboxyl group in the cyclic salicylates, in contrast to that in free salicylic acid, does not split off under these conditions. The complex-forming element, in addition to increasing the reactivity in the nitrosation reaction, by virtue of its positive charge prevents the transfer of the free electron pair from the carboxyl oxygen to the nucleus, and splitting off of CO_2. This second function of the complex-forming element can also be achieved by a proton, which results in a greater stability in the bond between the carboxyl group and the aromatic nucleus in a strongly acidic medium. Consequently, on reacting salicylic acid with nitrous acid in a medium of concentrated sulfuric acid, 3-nitrosalicylic acid or 5-nitrosalicylic acid are formed, depending on the reaction conditions [10]. In spite of the rigorous reaction conditions only an insignificant proportion of the salicylic acid reacts with splitting off of CO_2.

Although increasing the hydrogen ion concentration also leads to greater stability of the bond between the carboxyl group and the nucleus, in view of the depression of dissociation of the phenolic hydroxyl, salicylic acid has a considerably lower activity under these conditions in comparison with its intramolecularly ionized cyclic salts.

The cyclic salt of 5-nitrosalicylic acid formed, reacts further with nitrous acids to form the corresponding salt of 5-diazosalicylic acid. In this connection the composition of the reaction product varies with changes in the amount of nitrous acid introduced: with equimolecular proportions of salicylic and nitrous acids the nitroso compound is formed in 60-70% yield and the diazo compound in 10-12% yield depending on the cyclic salt taken; furthermore 20-28% of the salicylic acid remains unchanged. Increasing the amount of nitrous acid to 5.5 moles per 1 mole of salicylic acid results in the formation of only 5-diazosalicylic acid in over 90% yield.

EXPERIMENTAL

Reaction between cyclic aluminum salicylate and nitrous acid. To 8.0 g (0.050 g-mole) sodium salicylate dissolved in 50 ml water 14.5 g (0.060 g-mole) $AlCl_3 \cdot 6H_2O$ in 100 ml water was added. The pH of the solution was found before mixing to be 8.0 and 3.2, respectively; as a result of complex formation the pH of the mixture fell to 2.7. To the mixture obtained a solution of 3.8 g (0.055 g-mole) of sodium nitrite in 25 ml water was added and the resulting mixture was allowed to stand in the dark for 24 hrs at 20°. A 10% solution of hydrochloric acid was then added to give a faint reaction to Congo. Nitrous acid was not detected. The solution was transferred to a 500 ml measuring flask and made up to the mark with water.

The presence of the nitroso compound among the reaction products was confirmed by a qualitative test carried out according to [11]. Also the formation of azo compounds by azo coupling with alkaline solutions of resorcinol and 1,8-aminonaphthol-3,6-disulfonic acid indicated the presence of the diazo compound (11.2% calculated on the salicylic acid). The diazo compound was determined by the quantity of nitrogen evolved on boiling an aliquot portion of the solution with a cuprous chloride solution acidified with hydrochloric acid [12].

For determination of the nitroso compound content 0.25 g resorcinol dissolved in 25 ml of 10% sodium carbonate solution was added to 25 ml of the above solution and the azo compound formed was titrated with a vanadous sulfate solution [13]. The nitroso compound content, determined from the difference between the total azo and nitroso compound content and that of the diazo compound, was 63.8%.

If after the addition of 3.8 g of sodium nitrite to the reaction mixture the addition of $NaNO_2$ is continued so as to give a total quantity of 19.0 g (0.275 g-mole) over a period of 8-10 hrs, with simultaneous addition of concentrated hydrochloric acid to maintain a faint reaction to Congo, then only 5-diazosalicylic acid is formed. Its yield, determined by the same method [12] after removal of excess nitrous acid by the addition of sulfaminic acid, was 90.8%. Evaporation of an aliquot part of the reaction mixture in vacuo and acidification of the dry residue with 10% hydrochloric acid yielded 5-diazosalicylic acid, identified by the absorption spectra of the azo compounds formed with resorcinol and 1,8-aminonaphthol-3,6-disulfonic acid.

For determination of the amount of CO_2 evolved the reaction mixture was connected to a potash bulb and the gases evolved were absorbed in KOH solution. The absence of CO_2 in the absorbed gases was confirmed by a negative reaction with $Ba(OH)_2$.

Reaction between cyclic zinc salicylate and nitrous acid. When in the previous example 17.0 g (0.050 g-mole) zinc chloride was taken in place of aluminum chloride the quantities of diazo and nitroso compounds formed were 11.8% and 60.8%, respectively. On increasing the quantity of $NaNO_2$ to 19.0 g (0.275 g-mole) the nitroso compound was absent from the reaction mixture. The yield of diazo compound was 90.5%. The diazo compound was isolated and identified as 5-diazosalicylic acid in the same manner as in the previous example.

Reaction of cyclic chromium salicylate with nitrous acid. To 8.0 g (0.050 g-mole) sodium salicylate dissolved in 50 ml of hot water 50 ml of a solution containing 16 g $CrCl_3 \cdot 6H_2O$ was added and 25 ml of 10% sodium carbonate solution was then added with stirring. The mixture was then heated to boiling and refluxed for 1 hr. 75 ml of water was next added, the mixture cooled to 20° and further treated as in the previous examples. The addition of 3.8 g (0.055 g-mole) sodium nitrite yielded 69.4% of 5-nitrososalicylic acid and 9.8% of 5-diazosalicylic acid. On increasing the quantity of added sodium nitrite to 19.0 g (0.275 g-mole) with simultaneous addition of concentrated hydrochloric acid to maintain a faint reaction to Congo, only 5-diazosalicylic acid was formed in 92.6% yield.

SUMMARY

Cyclic salts of salicylic acid under conditions favoring their intramolecular dissociation possess high activities in the nitrosation reaction in comparison with salicylic acid. At the same time the complex formation suppresses the splitting off of CO_2, which occurs when salicylic acid reacts with nitrous acid.

It is shown that by the interaction of cyclic salts of salicylic acid with equimolar quantities of nitrous acid 5-nitrososalicylic acid is formed in 60-70% yield together with a small quantity of 5-diazosalicylic acid (10-12%). Increasing the quantity of nitrous acid to 5 moles leads to the formation of only 5-diazosalicylic acid in 90-93% yield.

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Received March 16, 1957

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DIMETHYL ARYLSULFON-N-METHYLAMIDOPHOSPHATES

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A large number of diesters of arylsulfonamidophosphoric acids have recently been prepared [1]. It is assumed, though not proved, that they have the amide structure (I). However, the possibility is not excluded that compounds of type (I) exist in equilibrium with the phosphazo form (II).

$$\underset{(I)}{ArSO_2NH{-}PO(OR)_2} \rightleftarrows \underset{(II)}{ArSO_2N{=}P(OR)_2(OH)}$$

To decide the question of the structure of diesters of arylsulfonamidophosphoric acids by chemical means is scarcely possible and for elucidation of their structure by physical means it is necessary to have, as reference samples, substances known to have structures (I) and (II). Many substances of structure (II) are known [1, 2] but there are no compounds authentically known to have structure (I). It was therefore of interest to carry out alkylation of the silver and sodium salts of diesters of arylsulfonamidophosphoric acids. By this means it would be possible to decide whether phosphazo compounds or esters of N-alkylated arylsulfonamidophosphoric acids are produced, since cases are known where alkylation of silver and sodium salts takes place in one case on the nitrogen and in the other case on the oxygen atom.

With this objective we investigated the methylation of silver and sodium salts of dimethyl arylsulfonamidophosphates. The sodium salts could not be methylated successfully. On prolonged heating with methyl iodide on a boiling water bath the sodium salts remained unchanged and with dimethyl sulfate they formed substances with unpleasant odors. The silver salts, on the other hand, reacted readily with methyl iodide forming dimethyl arylsulfon-N-methylamidophosphates.

$$ArSO_2NAg{-}PO(OCH_3)_2 + CH_3I \longrightarrow AgI + ArSO_2N(CH_3){-}PO(OCH_3)_2$$

By this means the N-methyl derivatives of dimethyl arylsulfonamidophosphates were prepared.

$$ArSO_2N(CH_3){-}PO(OCH_3)_2,$$

where $Ar = o\text{-}CH_3C_6H_4,\ \alpha\text{-}C_{10}H_7,\ \beta\text{-}C_{10}H_7.$

All of these are neutral materials, insoluble in alkalis. On prolonged boiling with aqueous-alcoholic hydrochloric acid solution they are hydrolyzed to N-methylarylsulfonamides, which indicates their structure.

$$ArSO_2N(CH_3){-}PO(OCH_3)_2 + H_2O \xrightarrow{H^+} ArSO_2NHCH_3$$

The N-metnyl derivatives dissolve readily in methyl iodide, acetone, benzene and hot alcohol, with difficulty in petroleum ether and are insoluble in water.

The dimethyl esters of α- and β-naphthylsulfon-N-methylamidophosphoric acids are crystalline materials with melting points of 91 and 82°, respectively. The melting points of the isomeric trimethyl esters are 84-85° and 93-94°, respectively [1].

Dimethyl o-tolylsulfon-N-methylamidophosphate was not obtained in the pure state: the reaction product could not be distilled without decomposition to a viscous, oily liquid.

EXPERIMENTAL

Preparation of the silver salts of the dimethyl arylsulfonamidophosphates. To a solution of 0.01 g-mole of the sodium salt of the dimethyl arylsulfonamidophosphate in 10-20 ml water an equimolar quantity of silver nitrate was added and the solution was allowed to stand overnight. The crystalline silver salt that separated was isolated and crystallized from water or alcohol. All operations of separation and purification were necessarily carried out in artificial light.

α-$C_{10}H_7SO_2NAg-PO(OCH_3)_2$. Yield 3.71 g (87.9%). Large prisms (from alcohol), dissolving easily in hot water, with difficulty in cold water and in alcohol; m. p. 155-157°.

Found %: Ag 25.39; OCH_3 14.47. $C_{12}H_{13}O_5NSPAg$. Calculated %: Ag 25.26; OCH_3 14.71.

β-$C_{10}H_7SO_2NAg-PO(OCH_3)_2$. Yield 4.18 g (99.1%). Small prisms (from water), m. p. 159-160°.

Found %: OCH_3 14.35. $C_{12}H_{13}O_5NSPAg$. Calculated %: OCH_3 14.71.

o-$CH_3C_6H_4SO_2NAg-PO(OCH_3)_2$. Yield 3.38 g (87.5%). The salt dissolved comparatively easily in cold water, very easily in hot water. Decomposes readily (particularly in a moist condition) in sunlight; m. p. 182-183°.

Preparation of the dimethyl N-methylamidophosphates. 0.02 g-mole of the silver salt and 20 ml methyl iodide were refluxed for 5-6 hrs. Silver iodide and the unreacted silver salt were filtered off and the filtrate evaporated. The oily liquid obtained in the case of the α- and β-naphthyl derivatives gradually crystallized out.

Dimethyl α-naphthylsulfon-N-methylamidophosphate. Yield of crude product 6.27 g (95.2%). Long prisms (from carbon tetrachloride) with m. p. 91°.

Found %: OCH_3 18.81, 18.91. $C_{13}H_{16}O_5NSP$. Calculated %: OCH_3 18.85.

Dimethyl β-naphthylsulfon-N-methylamidophosphate. Yield 4.42 g (67.0%). Long, thin, lustrous needles (from petroleum ether) with m. p. 82°.

Found %: OCH_3 18.90. $C_{13}H_{16}O_5NSP$. Calculated %: OCH_3 18.85.

Dimethyl o-tolylsulfon-N-methylamidophosphate. Yield 2.30 g (78.5%). Viscous oil, decomposes on distillation. Freed from a considerable amount of impurities by treatment with boiling petroleum ether.

Found %: OCH_3 20.65. $C_{10}H_{16}O_5NSP$. Calculated %: OCH_3 21.18.

Hydrolysis of dimethyl α-naphthylsulfon-N-methylamidophosphate. 0.822 g of the dimethyl ester, 10 ml alcohol and 10 ml 2N hydrochloric acid were refluxed for 20 hrs. The hot mixture was freed from a small quantity of oily droplets and left to crystallize for 24 hrs. Yield of N-methyl-α-naphthalenesulfonamide 0.35 g (63.3%). The melting point of 136° agrees with that in the literature [3].

SUMMARY

Dimethyl arylsulfon-N-methylamidophosphates, isomeric with the trimethoxyphosphazosulfonaryls, have been synthesized.

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Received March 18, 1957

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* Original Russian pagination. See C. B. translation.

ALKALOIDS OF PEGANUM HARMALA L.

II. THE STRUCTURE OF TWO NEW ALKALOIDS

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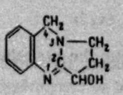
The isolation of peganine (I), harmine and two new bases designated as alkaloid No. 1 ($C_{11}H_{10}ON_2$) and alkaloid No. 2 ($C_{11}H_{10}O_2N_2$) from the parts of the rue (peganum harmala L.) growing above ground,has been reported earlier [1].

Continuing the investigation of the structure of the newly isolated substances reported in that communication we have found that on reduction of alkaloid No. 1 with lithium aluminum hydride dihydrodesoxypeganine ($C_{11}H_{14}N_2$) [2, 3] is formed. The occurrence of a bond at 1675 cm^{-1} (amide carbonyl) in the infrared absorption spectrum of alkaloid No. 1 enables the assumption to be made that it is an oxo derivative of desoxypeganine [2, 4]. According to its constants and elementary analysis alkaloid No. 1 is identical with 2,3-trimethylele-quinazolone-4 (II), which is described in the literature [4]. The identity of these substances was shown by a direct comparison of the two.

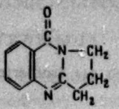
The infrared absorption spectrum of alkaloid No. 2 shows that this substance contains an hydroxyl group in addition to carbonyl amide. This suggests that alkaloid No. 2 is an oxo derivative of peganine, namely L-2,3-(α-hydroxytrimethylene)-quinazolone-4 (III). The racemate of this material, obtained by the oxidation of DL-peganine with hydrogen peroxide, has been described in the literature [4, 5]. L-2,3-(α-hydroxytrimethylene)-quinazolone-4,which we synthesized from L-peganine by the same method, was identical with alkaloid No. 2.

Thus, we have shown that the parts of the rue (Peganum harmala L.) growing above ground contain, in addition to peganine, substances that are either products of its decomposition or its precursors in the process of this alkaloid in the plant. The solution of the problem of the role which these substances play in the processes of transformation of peganine could probably be found by a study of the relationship of all three 2,3-trimethylenequinazoline derivatives in the various stages of vegetation of the plant.

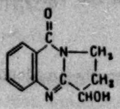
It is interesting to note that by reduction of 2,3-(α-hydroxytrimethylene)-quinazolone-4 with zinc in dilute hydrochloric acid, 2,3-trimethylenequinazolone-4 and desoxypeganine were obtained.



(I)



(II)



(III)

EXPERIMENTAL

Reduction of alkaloid No. 1 with lithium aluminum hydride. 2 g alkaloid No. 1 and 1 g $LiAlH_4$ in 150 ml anhydrous ether were refluxed for 7 hrs. Excess $LiAlH_4$ was decomposed by the addition of 3 ml water and 40 ml of a 10% solution of NaOH and 25 ml of a saturated solution of Seignette's salt (potassium sodium tartrate). The ether layer was separated and the alkaline suspension was exhaustively extracted with ether. After evaporation of the dried ethereal solution 1.53 g of material was obtained. Recrystallization from petroleum ether removed 0.3 g of unchanged alkaloid No. 1. The mother liquor was evaporated in vacuo; from the residue (0.95 g) a substance with m. p. 69-70° was obtained after repeated recrystallization from ether; R_f 0.51 (system I*, developer – Dragendorff's reagent) and 0.32 (system II, developer as above).

Found %: C 75.85; H 7.99; N 16.07. $C_{11}H_{14}N_2$. Calculated %: C 75.82; H 8.10; N 16.08.

Admixture with dihydrodesoxypeganine, prepared by reduction of peganine with sodium in amyl alcohol [3], gave no depression of the melting point.

Oxidation of L-peganine to L-2,3-(α-hydroxytrimethylene)-quinazolone-4 by hydrogen peroxide. 1 g L-peganine, 13 ml acetone and 10 ml 30% H_2O_2 were heated for 2 hrs at 55°. The solution was evaporated in vacuo to 5 ml, made alkaline with ammonia and extracted with chloroform. The residue after distilling off the chloroform was treated with 5 ml anhydrous ether and the solid residue (0.62 g) filtered off. After recrystallization from methanol the product had m. p. 202-203°; $[\alpha]^{18}D$ 128.9° (c 0.7; $CHCl_3$); R_f 0.70 (system II, developer – a solution containing 1% $KMnO_4$ and 1% Na_2CO_3).

Found %: C 65.54; H 4.85; N 13.61. $C_{11}H_{10}O_2N_2$. Calculated %: C 65.33; H 4.98; N 13.85.

No depression of the melting point was observed on mixing with alkaloid No. 2. The infrared spectra of the two materials coincided.

Reduction of alkaloid No. 2 with zinc dust in hydrochloric acid. A solution of 3.0 g alkaloid No. 2 in 100 ml 10% HCl was stirred with 10 g zinc dust for 8 hrs (20°). Excess zinc was filtered off and washed with water. The filtrate was made alkaline with ammonia and extracted with chloroform. The chloroform extract was evaporated to 50 ml and passed through a column containing 100 g Al_2O_3. On washing out with chloroform 1.05 g of a semicrystalline material was isolated, giving 0.67 g of a crystalline hydrochloride of m. p. 250-251° (from methanol) by treatment with an alcoholic HCl solution. The base obtained from the hydrochloride in the usual way had m. p. 109.5-110.5 (from petroleum ether), R_f 0.83 (system II, developer – Dragendorff's reagent).

Found %: C 71.26; H 5.49. $C_{11}H_{10}ON_2$. Calculated %: C 70.95; H 5.41.

The mixed melting point with 2,3-trimethylenequinazolone-4, prepared by oxidation of desoxypeganine with hydrogen peroxide [4], was 109.5-110.5°.

The filtrate after separation of the crystalline hydrochloride was diluted with anhydrous ether. The residue (0.27 g) which precipitated was purified by repeated solution in alcohol and precipitation with ether. This material then had m. p. 254°.

Found %: Cl 16.97. $C_{11}H_{12}N_2 \cdot HCl$. Calculated %: Cl 16.99.

A base with m. p. 87-88° (from ether) was obtained from the hydrochloride, R_f 0.19 (system II, developer – Dragendorff's reagent); a mixed melting point with desoxypeganine [4] gave no depression.

SUMMARY

Alkaloids No. 1 and No. 2 isolated previously from the parts of Peganum harmala L. growing above ground are identical with 2,3-trimethylenequinazolone-4 and L-2,3-(α-hydroxytrimethylene)-quinazolone-4, respectively. The presence of these compounds in a plant has been established for the first time.

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Received April 13, 1957

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* See comunication I [1] for the composition of the solvents (system I and system II).

** Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF INDOLE DERIVATIVES*

V. THE PROBLEM OF THE MECHANISM OF THE FISCHER REACTION

N. N. Suvorov, N. P. Sorokina, and Iu. N. Sheinker

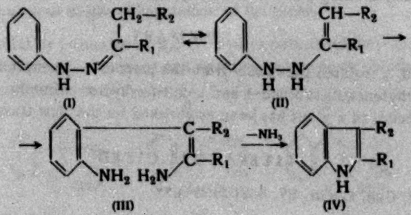
The conversion of arylhydrazones of carbonyl compounds to indole derivatives (the Fischer reaction) is an important and the most general method of preparing the latter. There are two methods of carrying out this reaction; the first of these, due to Fischer [2] proposes the use of condensing media of an acidic nature (mineral acids, anhydrous zinc chloride, boron trifluoride, etc.) in a quantity of at least 1 mole per mole of arylhydrazone, but in practice needing a large excess; the second is the method of A. E. Arbuzov [3] — comprising catalytic decomposition of the arylhydrazones. In both cases the formation of the indole derivative is accomplished by the separation of a molecule of ammonia (in the case of the Fischer method in the form of an ammonium salt) from the arylhydrazone molecule resulting from a preliminary intramolecular rearrangement in the latter.

Sound views on the mechanism of this interesting reaction were first developed by Brunner [4], whose work has remained completely unnoticed. The modern treatment of the mechanism of this reaction is connected in the chemical literature with the names of G. and R. Robinson who proposed in 1918, independently of Brunner, an analogous scheme, basing it on a number of indirect considerations [5]. The English investigators consider that the conversion of an arylhydrazone to an indole derivative consists of 3 stages:

1) tautomeric conversion of the arylhydrazone (I) to the corresponding unsaturated hydrazine (II),

2) ortho-benzidine rearrangement of the hydrazo compound (II) to the unsaturated diamine (III),

3) formation of the indole ring (IV) resulting from the elimination of a molecule of ammonia.



It should be mentioned that a number of other explanations of the Fischer reaction have been suggested [6-9]; however, they are inconsistent with the experimental facts and will not be considered here.

The most conclusive confirmation of the Robinson scheme is given by investigations carried out with the help of phenylhydrazine with "labeled" nitrogen N^{15} [10, 11]; this scheme requires for the formation of N-substituted indoles, readily obtained by the Fischer reaction from assymmetric alkyl (aryl) phenylhydrazones, the

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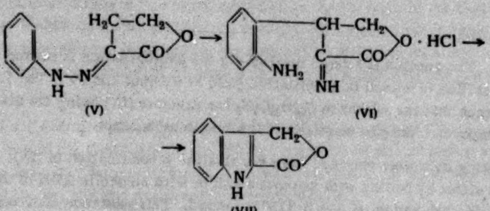
[*] For previous communications in this series see [1]. The present paper was read at the meeting of the Section of Organic Chemistry of the Moscow Section of the D. I. Mendeleev All-Union Chemical Society on March 11, 1957.

elimination of the nitrogen atom furthest away from the benzene nucleus, which was also established by means of labeled nitrogen. However, there is no direct evidence based on isolation of the two intermediate products (the unsaturated hydrazine (II) and the diamine (III)). For this reason attempts have been made, though not on a sufficiently sound basis, to cast doubt on the mechanism of the Fischer reaction suggested by G. and R. Robinson [12].

Only one example is known of the isolation of an intermediate product in a Fischer reaction. In 1950 Plieninger by passing gaseous hydrogen chloride into a solution of α-keto-γ-butyrolactone phenylhydrazone (V) in galcial acetic acid succeeded in obtaining a compound to which the structure α-imino-β-(2-aminophenyl)-γ-butyrolactone hydrochloride (VI) was ascribed [13]. Later it was shown that (VI) on heating with hydrochloric acid gives the corresponding indole derivative (VII) [14].



(V) (VI) (VII)

It should be noted however that the structure of compound (VI) was not definitely proved since for this purpose a reaction was used (acetylation with acetic anhydride in pyridine), which does not exclude the possibility of isomerization.

We felt that by carrying out the Fischer reaction in acetic anhydride it should be possible to detect the intermediate product in the acetylated form and thus to obtain direct evidence of the correctness of G. and R. Robinson's scheme. Methylethyl ketone phenylhydrazone, which very readily and in excellent yield gives 2,3-dimethyl- under the conditions of the Fischer reaction, was chosen as the material for investigation. Having the objective of isolating the acetylated intermediate product we decided to carry out the reaction under the conditions normally used for the preparation of enol acetates of ketones, since there is a definite parallelism between the formation of the unsaturated hydrazo compound (II) and the enolization of carbonyl compounds, as was noted at the time by the Robinsons. On refluxing methylethyl ketone phenylhydrazone (VIII) with acetic anhydride in the presence of catalytic quantities of p-toluenesulfonic acid (or with an equimolar quantity in the cold) a crystalline substance, with the composition $C_{14}H_{18}O_2N_2$ and m. p. 57-58°, is formed in 87% yield. This substance contains two acetyl groups, one double bond (shown by catalytic hydrogenation and by bromine addition) and contains no active hydrogen. On boiling for a short time with dilute mineral acids it gives 2,3-dimethylindole and can therefore be regarded as an intermediate product in the formation of the latter. 2,3-Dimethylindole is formed also by distilling this diacetyl derivative with zinc dust. The data obtained enable the structure 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 (IX) or the isomeric 2-acetylamino-3-(o-acetylaminophenyl)-butene-2 (X) to be assigned to the compound $C_{14}H_{18}O_2N_2$. In order to choose between these two structures the infrared spectrum of this compound was examined. In the infrared spectrum (Fig. 1) there is no absorption band in the region 3000-3400 cm^{-1} indicating the absence of an N—H bond from the compound. In the region characteristic of double bonds there are two almost coincident, intensive bands at 1690 and 1664 cm^{-1} corresponding to the two amide carbonyl groups C=O, evidently differing somewhat because of their position in the molecule. Again at 1592 cm^{-1} there is a band of low intensity caused by the aromatic system of double bonds of the benzene nucleus. The absence from the spectrum of the band characteristic of the N—H bond (3000-3400 cm^{-1}) eliminates structure (X) for the compound in question, which differs from the other by the presence of two N—H bonds in the molecule.

Definite evidence for the structure of the compound with m. p. 57-58° was obtained by a study of its catalytic hydrogenation. An attempt to rupture the N—N bond presumed to be present was unsuccessful: on hydrogenation in an autoclave at 42 atmos and 60° for a period of 7 hrs in the presence of a very large quantity of Raney nickel (W-4) reduction of only the double bonds occurred and it was not possible to find even a trace of aniline

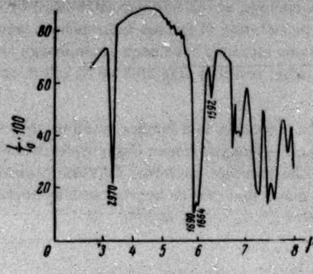


Fig. 1.

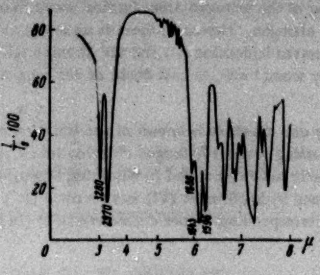


Fig. 2.

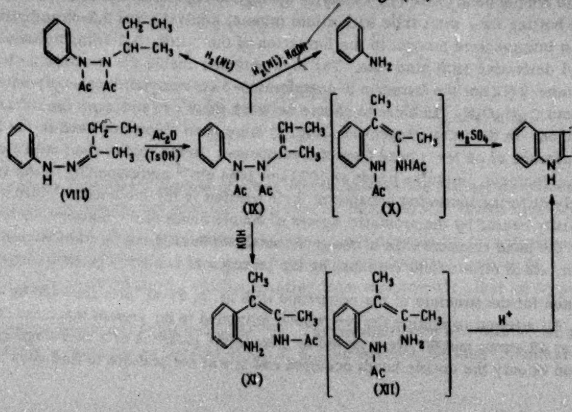
in the reaction product. The position is altered markedly if the hydrogenation is carried out in an alkaline medium. In these circumstances aniline is formed in quantitative yield at 6 atmos and 80°. The formation of the latter provides indisputable evidence that the substance $C_{14}H_{18}O_2N_2$ has structure (IX) being the diacetyl derivative of the unsaturated hydrazo compound – the first stage (II) of the Robinsons' scheme.

Extremely interesting data were obtained from the alkaline saponification of (IX). In this case no 2,3-dimethylindole is formed either by boiling with aqueous alkali or with alcoholic KOH in the cold, but a substance with the composition $C_{12}H_{16}ON_2$ and m. p. 114.5-115° is formed. This substance contains one acetyl group and active hydrogen and gives a positive isonitrile reaction for a primary amino group.

In the infrared spectrum of this compound (Fig. 2) there is an intensive N–H band at 3280 cm^{-1} and in the region characteristic of double bonds there is a system of three intensive bands: of these, the band at 1686 cm^{-1} is a typical amide band, the band at 1643 cm^{-1} can be related to the deformation vibration of NH_2 groups and that at 1596 cm^{-1} to vibration of the aromatic system of double bonds, the considerable increase in intensity in this case results from the presence of additional conjugation (for example, from a C=C bond outside the nucleus).

2,3-Dimethylindole is formed instantaneously by the action of dilute acids on the compound of m. p. 114.5-115° in the cold. This reaction takes place so easily that attempts to diazotize this compound were unsuccessful: closing of the indole ring occurs so rapidly that the diazo compound cannot be formed. 2,3-Dimethylindole is also obtained together with acetamide on heating the above compound to 150°.

All these data indicate conclusively that the substance of m. p. 114.5-115° is 3-acetylamino-2-(o-aminophenyl)-butene-2 (XI). Formula (XII) is excluded by the stability of the substance under conditions of alkaline saponification, and also because cyclization of (XII) would lead to 1-acetyl-2,3-dimethylindole. Compound (XI) is the acetyl derivative of an unsaturated diamine – the second stage (III) of the Robinsons' scheme.



We have thus succeeded in bringing about an ortho-benzidine rearrangement of the unsaturated hydrazocompound (IX) to the diamine (XI) in an alkaline medium. It should be noted that although the benzidine rearrangement takes place, as a rule, in acidic media, other cases have also been recorded in the literature. The case that has been investigated most is that of the rearrangement of 2,2-hydrazonaphthalene. In 1903 Meisenheimer and Witte [15] showed that on heating the latter with alcoholic alkali 2,2-diamino-1,1-dinaphthyl is formed, and this was explained by a benzidine rearrangement under the action of alkali [16]. Later, in papers by L. G. Krolik and V. O. Lukashevick [17] and by Shine [18] it was established that rearrangement in this case takes place without any chemical influence, probably by alcohol taking part as a catalyst. It is very probable that in our case also the alkali functions only to saponify one of the acetyl groups in (IX), as a result of which the stability of the molecule is broken down (see experiments on the hydrogenation of (IX) in neutral and alkaline media).

This loss of the stabilization imparted by the formation of the diacetyl derivative of the unsaturated hydrazocompound suggests a somewhat different line of investigation of the reaction in the case of asymmetric alkylphenylhydrazone. Thus, for example, the asymmetric methylethyl ketone methylphenylhydrazone on heating with acetic anhydride under the conditions described for the preparation of (IX) gives a mixture of at least two substances of which one $C_{13}H_{15}ON$ with m. p. 126.5-127.5° gives a picrate (m. p. 120.5-121.5°) and a 2,4-dinitrophenylhydrazone (m. p. 277-278°).

The formation of a 2,4-dinitrophenylhydrazone indicates the presence of a keto group in the molecule; at the same time the position of the C=O band in the infrared spectrum of this substance at 1660 cm^{-1} shows that this group occurs on the aromatic nucleus in the para position relative to the point of attachment of the nitrogen atom (cf. the spectra of the o-, m- and p-aminoacetophenones [19]).

In the infrared spectrum there is also a strong band at 1560 cm^{-1} which is normally found in N-heterocyclic compounds with bonds of an "aromatic" nature. All this enables the assumption to be made that this substance is a ketone of the indole series, possibly 5-acetyl-1,2,3-trimethylindole. Work on the study of the behavior of asymmetric methylethyl ketone alkylphenylhydrazones is continuing.

Thus by carrying out the Fischer reaction in acetic anhydride and saponifying the acetyl derivative of the unsaturated hydrazocompound we have succeeded in obtaining, in the acetylated form, both of the intermediate products of this reaction – the unsaturated hydrazine (II) and the unsaturated diamine (III) and the fact that these intermediate products cannot be isolated under the Fischer reaction conditions is explained by the extreme rapidity with which the indole ring forms from the unsaturated diamine (III) in an acidic medium. The case reported by Plieninger [13, 14] is probably explained by the fact that here the unsaturated diamine was precipitated in the form of a difficultly soluble hydrochloride. Our artificial method allowed the Fischer reaction to be "dissected" into three completely separate stages in agreement with the Robinsons' mechanism.

The necessity for a catalyst in the first stage of the Fischer reaction can evidently be considered to have been established since on heating methylethyl ketone phenylhydrazone without toluenesulfonic acid the reaction follows another course with the formation of the acetyl derivative of phenylhydrazine (cf. [20]). As regards the o-benzidine rearrangement the presence of an "acid catalyst" is not necessary in this case. The indole ring-closure reaction is very markedly accelerated in the presence of hydrogen ions but it can be accomplished also by heating sufficiently strongly in a neutral medium.

These considerations provide a good explanation of the catalytic conversion of arylhydrazones to indole derivatives by A. E. Arbuzov [3], and the adducts of hydrazo compounds with acetylenedicarboxylic esters of Diels [21]. It should be mentioned that there are in the literature two cases of the formation of indole derivatives from phenylhydrazones in alkaline media – 2-phenylindole from acetophenone phenylhydrazone on refluxing with a solution of sodium ethylate in alcohol [22] and 2-methylindole under the Kishner reaction conditions [23]. It must therefore be recognized that also the formation of the unsaturated hydrazine (II) is evidently not conclusively connected with the presence of an "acid type" catalyst. However, this assumption requires specific experimental verification.

EXPERIMENTAL

2-(N,N'-Diacetyl-β-phenylhydrazino)-butene-2 (IX). 25 g (0.154 mole) methylethyl ketone phenylhydrazone (b. p. 147-147.5° at 15 mm) was refluxed for 1 hr with 159 g (147 ml, 1.54 moles) acetic anhydride and 0.636 g (0.0037 mole, ~ 2.5 mole%) p-toluenesulfonic acid monohydrate. 0.3 g of crystalline sodium acetate was added to the hot solution, the acetic anhydride distilled off in vacuo, the residue treated with 80 ml water and the product extracted with ether (4 times with 100 ml). After drying over anhydrous sodium sulfate the ether was distilled off and the residue redistilled in vacuo, a fraction being collected at 167-169° at 1.5 mm. The oil obtained (29.62 g) was dissolved in 15 ml absolute ether, 15 ml hexane was added and the product crystallized at −18°. 27 g (86.8%) of a pale pink crystalline material with m. p. 52-56° was obtained. After recrystallization (from n-hexane or absolute ether) a colorless substance was obtained that became pink on standing. M. p. 57-58°. Fairly good solubility in water, good solubility in alcohol, chloroform and benzene; moderately soluble in ether, dissolves with difficulty in cold n-hexane. Decolorizes bromine water and dilute potassium permanganate solution; gives a negative reaction with Fehling's solution.

Found %: C 68.11, 68.01; H 7.15, 7.00; N 10.84, 10.85; Ac 34.3. $C_{14}H_{18}O_2N_2$. Calculated %: C 68.29; H 7.31; N 11.38; Ac 34.9. No active H detected (Zerewitinoff method).

Acid hydrolysis of the diacetyl derivative (IX). 1 g of 2-(N,N'-diacetyl-β-phenylhydrazono)-butene-2 was refluxed with 15 ml of an aqueous solution (1 : 1) of sulfuric acid for 30 min. On cooling the precipitated material was extracted with ether. After distilling off the latter 0.5 g (85%) of 2,3-dimethylindole was obtained, m. p. 99-102° (from aqueous alcohol). No depression of the melting point was observed on mixing with an authentic sample.

Catalytic hydrogenation of (IX). a) 8 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 was hydrogenated in an autoclave over 8 g Raney nickel (W-4) in 100 ml ethyl alcohol at 42 atmos and 60° for 7 hrs. After working up in the usual way and redistilling in vacuo, 7.8 g of a colorless oil was obtained, b. p. 151-155° (1.5 mm). From the results of elementary analysis it was 2-(N,N'-diacetyl-β-phenylhydrazino)-butane.

Found %: C 67.25, 67.15; H 8.09, 8.19; N 11.06, 11.05. $C_{14}H_{20}O_2N_2$. Calculated %: C 67.74; H 8.06; N 11.29.

b) 2.5 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 was hydrogenated in an autoclave over 2.5 g Raney nickel (W-4) in a mixture of 20 ml ethyl alcohol and 95 ml of 5% aqueous sodium hydroxide. Pressure 6 atmos, temperature 80°, hydrogenation time 2 hrs. The catalyst was filtered off and the filtrate steam-distilled. The distillate was saturated with sodium chloride and the product extracted with ether. To the residue after distilling off the ether 2.5 ml acetic anhydride and 20 ml water was added. 1.32 g (96%) of a substance with m. p. 112-114° was obtained that gave no depression of the melting point on mixing with an authentic sample of acetanilide.

3-Acetylamino-(2-o-aminophenyl)-butene-2 (XI). a) 3 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 (IX) was refluxed for 2 hrs with 30 ml of a 5% aqueous sodium hydroxide solution. On cooling the mixture was diluted with 50 ml water and the product extracted with ether. After distilling off the latter 2.3 g (92.5%) of an oil, that crystallized rapidly, was obtained. M. p. 114.5-115° (from 1 : 1 alcohol−water). The product was practically insoluble in water and dissolved readily in the usual organic solvents.

Found %: C 70.45, 70.15; H 7.77, 7.91; N 13.94, 13.28; Ac 21.3; active H (Zerewitinoff method) 0.31, 0.51. $C_{12}H_{16}ON_2$. Calculated %: C 70.50; H 7.84; N 13.72; Ac 21.18; active H 0.49.

b) 0.5 g of the diacetyl derivative (IX) was dissolved in 5 ml of 5% alcoholic potassium hydroxide and kept at room temperature for 24 hrs. The solution was then poured into water and extracted with ether. 0.4 g (95%) of 3-acetylamino-2-(o-aminophenyl)-butene-2 was obtained. M. p. 114-114.5° (from aqueous alcohol).

Conversion of 3-acetylamino-2-(o-aminophenyl)-butene-2 (XI) to 2,3-dimethylindole. a) To a solution of 0.5 g (XI) in 10 ml ethyl alcohol 1 ml of concentrated hydrochloric acid was added. The characteristic order of 2,3-dimethylindole arose immediately. After 5 min 20 ml water was added and the 2,3-dimethylindole was extracted with ether. Yield 0.32 g (90%). M. p. 104.5-106° (from aqueous alcohol). No depression of the melting point was observed on mixing with an authentic sample.

b) To a hot solution of 2 g of the monoacetyl derivative (XI) in 10 ml alcohol, 1 drop of concentrated hydrochloric acid was added. The odor of 2,3-dimethylindole arose instantly. After refluxing for 1 hr the solution was diluted with 40 ml water and the 2,3-dimethylindole was carefully extracted with ether. The ethereal extract was washed with water which was combined with the main aqueous layer. The water was distilled off in vacuo and the residual oil redistilled. B. p. 218-220°. 0.45 g (78%) of acetamide was obtained. After distilling off the ether 1.28 g (91%) of 2,3-dimethylindole was obtained. M. p. 104-106°.

c) 1.4 g 3-acetylamino-2-(o-aminophenyl)-butene-2 was carefully heated in a Wurtz flask, with a thermometer immersed in the material. At about 150° a vigorous reaction suddenly commenced, the temperature rose spontaneously to 220° and a liquid distilled off that crystallized rapidly. This substance redistilled at 220° and had m. p. 81-82°. No melting point depression was observed with a sample of acetamide. Yield of acetamide 0.25 g (62%). The residue in the distillation flask was dissolved in ether and the product was sublimed in vacuo (1.5 mm). Yield of 2,3-dimethylindole 0.83 g (84%). M. p. 102-104.5°.

SUMMARY

1. By means of an artificial method (carrying out the Fischer reaction in acetic anhydride and saponifying the diacetyl derivative of the unsaturated hydrazine) the Fischer reaction has been successfully "dissected" into three stages, corresponding to the three stages (unsaturated hydrazo compound – unsaturated diamine – indole derivative) of the mechanism proposed by G. and R. Robinson.

2. Taking methylethyl ketone phenylhydrazone as an example both intermediate products have been isolated in the acetylated form, their structures were proved and the conditions for conversion to the indole derivative have been studied. Direct evidence has thus been obtained for the correctness of G. and R. Robinson's scheme.

3. It has been shown that the formation of the unsaturated hydrazine takes place in the presence of a catalyst of an acidic character; the ortho-benzidine rearrangement does not absolutely require the presence of such a catalyst but can take place in an alkaline medium; the formation of the indole ring proceeds very rapidly when catalyzed by hydrogen ions but it can also be accomplished thermally.

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Received April 13, 1957

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THE SYNTHESIS OF TROPANE-3-α-OL, TROPINE

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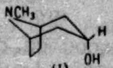
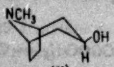
An important place among the alkaloids is occupied by representives of the tropane group – cocaine, atropine, tropine and also natural and synthetic derivatives. The presence of substituents on the pyrrolidine-piperidine grouping gives a wide possibility of the existence of tropane alkaloids in different stereoisomeric forms. Thus, for cocaine four configurations are known and correspondingly there are four racemic isomers. It has been established that allococaine, allopseudococaine and tropine, synthesized in 1956, are derivatives of tropane-3-α-ol, tropine (I) whereas the basis of natural cocaine and pseudococaine and pseudococaine is the pseudotropine structure (II) [1].



(I)



(II)

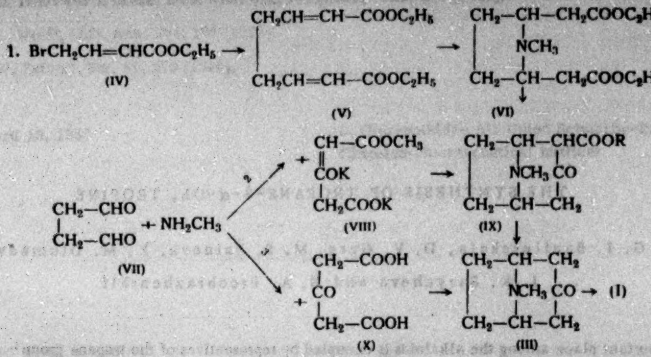
Both forms of tropanol-3 (I and II) have been prepared by a number of authors by reduction of the corresponding ketone, tropanone (III). As the investigations showed, in the formation of one isomer or the other an important role is played not only by the choice of hydrogenating agent but also by the reaction conditions. By the use of sodium amalgam pseudotropine (II) is formed in predominating quantity [2], whereas the use of zinc dust and hydriodic acid leads to a mixture of pseudotropine (II) and tropine (I) [3]. According to the patent literature electrochemical reduction on lead electrodes in an acidic medium gives pseudotropine (II) [4], and under analogous conditions but in an alkaline medium the reaction product is tropine (I) [5].

The present paper describes a stereo-directed reduction of tropanone (III) to tropine (I) accomplished by us. For the preparation of the starting material, previously published methods [6] were used, with the introduction of a number of modifications. We carried out the synthesis of tropanone (III) in accordance with three schemes.

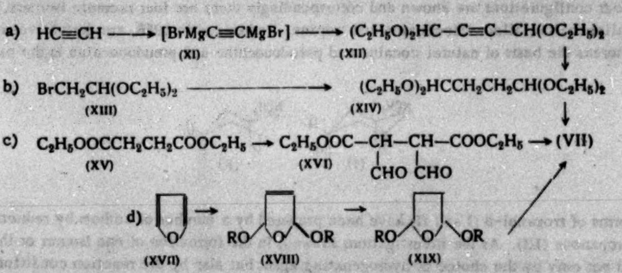
1. In contrast to P. Karrer and G. Alagil [6], who suggested this scheme, ethyl γ-bromocrotoniate (IV) was condensed to ethyl octadiene-2,6-dioate-1,8 (V) with a zinc-copper couple [7] and not with silver. Furthermore the ester of N-methylpyrrolidine-α,α'-diacetic acid (VI) was prepared directly from the ester (V) by the action of methylamine, eliminating the hydrogen bromide addition stage.

2. The method described in the literature for the preparation of the tropinonecarboxylic ester (IX), starting from succindialdehyde (VII), methylamine hydrochloride and the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII) [8], was improved by us in that we found a method of determining the end of the reaction by the formation of the reineckate. The conversion of the tropinonedicarboxylic acid ester was carried out by the usual method [9].

3. The method of G. Gal, I. Simonly and D. Tokar [10] was used to prepare tropinone (III) in one stage (see scheme on top of following page).


1. $BrCH_2CH{=}CHCOOC_2H_5$
(IV)
$CH_2CH{=}CH{-}COOC_2H_5$
$CH_2CH{=}CH{-}COOC_2H_5$
(V)
$CH_2{-}CH{-}CH_2COOC_2H_5$
NCH_3
$CH_2{-}CH{-}CH_2COOC_2H_5$
(VI)
$CH_2{-}CHO$
$CH_2{-}CHO$
(VII)
$+ NH_2CH_3$
$CH{-}COOCH_3$
COK
CH_2COOK
(VIII)
$CH_2{-}CH{-}CHCOOR$
NCH_3 CO
$CH_2{-}CH{-}CH_2$
(IX)
$CH_2{-}COOH$
CO
$CH_2{-}COOH$
(X)
$CH_2{-}CH{-}CH_2$
NCH_3 CO → (I)
$CH_2{-}CH{-}CH_2$
(III)

The succindialdehyde (VII) necessary for the synthesis of tropinone (III) we again prepared by a number of methods:


a) $HC{\equiv}CH \longrightarrow [BrMgC{\equiv}CMgBr] \longrightarrow (C_2H_5O)_2HC{-}C{\equiv}C{-}CH(OC_2H_5)_2$
(XI)
(XII)
b) $BrCH_2CH(OC_2H_5)_2 \longrightarrow (C_2H_5O)_2HCCH_2CH_2CH(OC_2H_5)_2$
(XIII)
(XIV)
c) $C_2H_5OOCCH_2CH_2COOC_2H_5 \longrightarrow C_2H_5OOC{-}CH{-}CH{-}COOC_2H_5 \longrightarrow$ (VII)
(XV)
(XVI)
CHO CHO
d)
RO
OR
(XVII)
(XVIII)
(XIX)

a) From Iotsich's complex (XI) by a method developed by one of us [11] into which improvements were introduced enabling the yield of succindialdehyde ethyl diacetal (XIV) to be increased.

b) For reacting bromoacetaldehyde ethyl acetal (XIII) with sodium, diethyl ether containing peroxidic compounds was used as solvent in accordance with published directions [12]. According to our observation, in spite of the reference quoted, keeping the reaction mass for more than 30 hrs leads to a lowering of the yield of succindialdehyde ethyl diacetal (XIV).

c) This method of synthesizing succindialdehyde was worked out by us for the first time. There is in the literature only an indication of an analogous scheme of synthesis [13].

d) It was found in the present work that in the preparation of dimethoxydihydrofuran (XVIII) the alkoxylation reaction [14] can be carried out in the absence of a solvent.

With the object of finding conditions for the stereo-directed reduction of tropinone (III) to tropine (I) we examined a number of methods – reduction with sodium amalgam, electrolytic and catalytic reduction under various conditions. Only by reduction with Raney nickel catalyst at 60 atmos and 20° did we succeed in preparing tropine (I) free from pseudotropine (II). This synthetic tropine was shown to be identical with tropine isolated from the natural alkaloid atropine.

EXPERIMENTAL

Ethyl octadiene-2,6-dioate-1,8 (V). To a suspension of 17.2 g of freshly prepared zinc-copper couple [7] in 28 ml anhydrous dioxan, heated to 80°, 2 ml of a solution of 40 g ethyl γ-bromocrotonate (IV) in 56 ml dioxan was added, together with a small crystal of iodine. After the appearance of a definite turbidity in the liquid (about 50 min) the remainder of the solution was added dropwise at 80-85°. The reaction mixture was then refluxed for

1.5 hr and treated with 100 ml sulfuric acid (d^{20}_4 1.032), after cooling to 0°. The precipitate was filtered off and washed with 100 ml water. The combined filtrates were extracted with 250 ml ether. The resulting extract was washed with 10% sodium thiosulfate solution, neutralized with a suspension of sodium bicarbonate in water and dried over sodium sulfate. The residue after the removal of ether was redistilled. Yield 4.92 g (20.9%).

B. p. 97-99° (0.3 mm), d^{20}_4 1.042, $n^{20}D$ 1.4604, MR_D 59.55. $C_{12}H_{18}O_4\ F_2$. Calculated 59.99. Found %: C 63.92; H 8.23. $C_{12}H_{18}O_4$. Calculated %: C 63.69; H 8.02.

Diethyl N-methylpyrrolidine-α,α'-diacetate (VI). Methylamine, dried over potassium hydroxide, was passed into 7 ml absolute ethyl alcohol to a weight increase of 0.30 g. 4.0 g diethyl octadiene-2,6-dioate-1,8 (V) dissolved in 5 ml ethyl alcohol was added to the solution obtained. The reaction mixture was kept at room temperature for 144 hrs. The solvent was then distilled off and the residue redistilled. Yield 2.9 g (63.7%).

B. p. 110-112° (0.33 mm), d^{20}_4 1.0740, $n^{20}D$ 1.4610, MR_D 65.70. $C_{13}H_{21}O_4N$. Calculated 65.28.

Ethyl tropinonecarboxylate (IX, R = C_2H_5). 2.0 g diethyl N-methylpyrrolidine-α,α'-diacetate (VI) was added dropwise over a period of 10 min to sodium ethylate prepared from 0.22 g sodium and 20 ml ethyl alcohol. The reaction mixture was refluxed for 2 hrs and then after cooling to 0° 20 ml of ice-water was added and the mixture was extracted with 150 ml ether. The aqueous layer was acidified with hydrochloric acid (d^{20}_4 1.047) and after extraction with 150 ml ether it was neutralized with sodium bicarbonate and extracted with 100 ml ether and 100 ml benzene. The combined extracts were dried over sodium sulfate. The solvent was distilled off. 0.9 g of the ethyl tropinonecarboxylate obtained was converted to the picrate. M. p. 133-135.5°.

Found %: N 12.85, 12.88. $C_{17}H_{20}O_{10}N_4$. Calculated %: N 12.75.

Acetylenedialdehyde ethyl diacetal (XII). Purified acetylene was passed for a period of 12 hrs through a solution of ethylmagnesium bromide prepared from 24.3 g magnesium and 76.2 ml ethyl bromide in 200 ml absolute ether. To the resulting grey mass 176 ml ethyl orthoformate was added over a period of 1 hr with vigorous stirring. A precipitate was formed to which 300 ml dry benzene was added. The ether was then distilled from the mixture obtained and the commencement of the reaction, which is accompanied by frothing, was awaited, whereupon the warming was discontinued. After 30 min the reaction mixture was cooled to 0°, treated with a saturated solution of ammonium chloride to pH 6 and extracted with 450 ml ether. The combined extracts were dried over potassium carbonate and redistilled after removal of the solvent. Yield 102 g (75.4% calculated on the magnesium).

B. p. 117-118° (7 mm), m. p. 21-22°, d^{20}_4 0.9586, $n^{20}D$ 1.4309, MR_D 62.10. $C_{13}H_{22}O_4\ F$. Calculated 62.18. Found %: C 62.48, 62.67; H 9.71, 9.71. $C_{13}H_{22}O_4$. Calculated %: C 62.57; H 9.71.

Succindialdehyde ethyl diacetal (XIV). 50.3 g acetylenedialdehyde ethyl diacetal (XII) was hydrogenated in 30 ml ethyl alcohol in the presence of 10 g Raney nickel catalyst at an initial pressure of 70 atmos and 24°. By the end of the reaction the pressure had fallen to 58 atmos. The catalyst was filtered off. The residue after the ether was distilled off, was redistilled. Yield 48.9 g (93.2%). B. p. 120-122° (20 mm).

Found %: C 61.24, 61.35; H 10.98, 11.30. $C_{13}H_{26}O_4$. Calculated %: C 61.48; H 11.19.

Succindialdehyde (VII) from succindialdehyde ethyl diacetal (XIV). 10 g succindialdehyde ethyl diacetal was stirred for 1 hr with 95 ml 0.1 N sulfuric acid. The solution was then neutralized with sodium bicarbonate, salted out with calcium chloride and extracted with 300 ml ether. The ethereal extract was dried over sodium sulfate. After removal of the solvent the residue was redistilled. Yield 1.3 g (34.8%).

B. p. 62-63° (12 mm), d^{20}_4 1.0624, $n^{20}D$ 1.4265, MR_D 20.80. $C_4H_6O_2$. Calculated 20.69.

Succindialdehyde ethyl diacetal (XIV) from bromoacetaldehyde ethyl acetal (XIII). To 10.6 g sodium wire, submerged in 200 ml absolute ether containing peroxidic compounds, 87 g bromoacetaldehyde ethyl acetal (XIII) [b. p. 58-60° (12 mm), d^{20}_4 1.3452, $n^{20}D$ 1.4592, MR_D 40.07] was added over a period of 2 hrs. The formation of a yellowish-brown precipitate, accompanied by the evolution of heat, was observed. After stirring for 48 hrs 100 ml ice-water was added to the reaction mixture to dissolve the precipitate. The upper layer was removed and the lower extracted with 100 ml ether. The combined extracts were treated with 50 ml of a 20% aqueous solution of ferrous sulfate, washed with 45 ml water and dried over calcium chloride. After distilling off the solvent the residue was redistilled. Yield 5.27 g (10.2%).

B. p. 116-117° (20 mm), d^{20}_4 0.9168, $n^{20}D$ 1.4151, MR_D 64.01; calculated 64.19. Found %: C 61.03, 61.26; H 11.32, 11.37. $C_{12}H_{26}O_4$. Calculated %: C 61.51; H 11.19.

Succindialdehyde (VII) from ethyl diformylsuccinate (XVI). To 36.7 g sodium wire under 150 ml dry toluene 140 g diethyl succinate (XV) (b. p. 114.5-118° for 25 mm) and 144 g ethyl formate were added over a period of 30 min. The mixture was allowed to stand at room temperature for 50 hrs, by which time the sodium had completely reacted with the compounds stated. 150 g crushed ice was then added to the reaction mixture over a period of 15 min causing the formation of two layers. The lower layer was separated and extracted with 300 ml toluene. The combined toluene extracts were washed with 150 ml ice-water and discarded. The aqueous part of the reaction mixture was neutralized with dilute (d^{20}_4 1.066) sulfuric acid. The precipitate was filtered off and extracted with 300 ml toluene. The toluene was distilled off from the extracts obtained. The residue (150 g) which was a heavy, light brown liquid was heated to boiling with a 20% aqueous oxalic acid solution in a current of nitrogen, omitting the purification stage. Evolution of carbon dioxide was observed. Heating was continued until the oily layer disappeared (4 hrs). The cooled reaction mixture was neutralized with a saturated aqueous sodium bicarbonate solution. The precipitate was filtered off, the filtrate saturated with calcium chloride, extracted with 400 ml ether and the combined extracts dried over sodium sulfate. The residue was redistilled after the solvent had been distilled off. Yield 8.9 g (13.1% calculated on the diethyl succinate).

B. p. 69.5-71° (25 mm), d^{20}_4 1.0659, $n^{20}D$ 1.4260, MR_D 20.65; calculated 20.69. Found %: C 55.63; H 7.04. $C_4H_6O_2$. Calculated %: C 55.80; H 7.02.

2,5-Dimethoxydihydrofuran (XVIII, R = CH_3). To a solution of 28.3 g furan (b. p. 31.5-32° at 756 mm) in 210 ml anhydrous methyl alcohol cooled to −40°, 73.5 g bromine dissolved in 300 ml methyl alcohol cooled to −40° was added dropwise with stirring. The addition was carried out at a rate such that the temperature of the reaction mixture did not exceed −25° (about 1 hr). After maintaining these conditions for 30 min a current of dry ammonia was passed into the reaction mixture to a pH of 6 and stirring was continued at −5° until the color disappeared (about 1 hr) after which ammonia was again passed in to pH 8. The methyl alcohol was distilled off in vacuo (20-30 mm). The precipitate that separated was filtered off and washed with 90 ml methylene dichloride. The residue was redistilled after removal of the solvent. Yield 39 g (72.1%).

B. p. 34-36° (3 mm), d^{20}_4 1.0730, $n^{20}D$ 1.4350, MR_D 31.65. $C_6H_{10}O_3$ F. Calculated 32.17. Found %: C 55.46, 55.14; H 7.48, 7.51; $C_6H_{10}O_3$. Calculated %: C 55.37; H 7.74.

2,5-Diethoxydihydrofuran (XVIII, R = C_2H_5). To a mixture of 34 g furan, 100 ml absolute ether and 150 ml absolute ethyl alcohol cooled to −35°, a solution of 28 ml bromine in 350 ml ethyl alcohol cooled to −40°, was added dropwise with stirring over a period of 1 hr, taking care that the temperature did not exceed −25°. After maintaining this temperature for 30 min dry ammonia was passed in to pH 6, stirring was continuedat −5° until the color disappeared and ammonia was again passed in to pH 8. The precipitate was filtered off and washed with 75 ml absolute ether. The residue was redistilled after removal of the solvent. Yield 54.9 g (69.5%).

B. p. 46-48° (5 mm), d^{25}_4 1.0017, $n^{25}D$ 1.4310, MR_D 40.86. $C_8H_{14}O_3$ F. Calculated 41.41. Found %: C 60.68, 61.05; H 8.56, 8.80. $C_8H_{14}O_3$. Calculated %: C 60.80; H 8.86.

2,5-Dimethoxytetrahydrofuran (XIX, R = CH_3). 126 g 2,5-dimethoxydihydrofuran (XVIII, R = CH_3) was hydrogenated in the presence of 13 g Raney nickel catalyst at room temperature and atmospheric pressure, with mechanical stirring. After 22 liters of hydrogen had been absorbed in 6-8 hrs the catalyst was filtered off and washed with 50 ml anhydrous methyl alcohol. The residue after the solvent was distilled off, containing 4-6% dimethoxytetrahydrofuran was combined with the main bulk and redistilled. Yield 109.4 g (85.5%).

B. p. 53-54° (22 mm), d^{25}_4 1.022, $n^{25}D$ 1.4158, MR_D 32.45; calculated 32.63. Found %: C 54.50, 54.49; H 9.11, 9.33. $C_6H_{12}O_3$. Calculated %: C 54.53; H 9.15.

2,5-Diethoxytetrahydrofuran (XIX, R = C_2H_5). Hydrogenation of 2,5-diethoxydihydrofuran (XVIII, R = C_2H_5) was carried out under the conditions used for the preparation of 2,5-dimethoxytetrahydrofuran. 44.2 g 2,5-diethoxydihydrofuran and 5 g Raney nickel catalyst were used. Yield 36.4 g (81.3%).

B. p. 67-69° (15 mm), d^{25}_4 0.9670, $n^{25}D$ 1.4173, MR_D 41.69; calculated 41.87. Found %: C 59.83, 58.73; H 10.05, 10.11. $C_8H_{16}O_3$. Calculated %: C 59.97; H 10.06.

Dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII). 46.8 g of the dimethyl ester of acetonedicarboxylic acid was added, with vigorous mechanical stirring, to a mixture of 240 g of 50% aqueous potassium hydroxide and 138 ml methanol cooled to −5°, whereupon the temperature of the reaction mixture rose spontaneously to 15°. Cooling was then discontinued and the temperature was brought to 25° in 20-30 min. After maintaining these conditions for 10 min the mixture obtained was again cooled to 0° and 45 ml ether was added. The precipitate that formed was filtered off, washed with 45 ml methanol and 100 ml ether cooled to 0° and dried in a vacuum desiccator. Yield 57.2 g (90.1%).

5.3 ml 0.1 N hydrochloric acid was required for the titration of 0.1 g of the substance obtained. After boiling the sample taken for neutralization for 30 min a further 2.9 ml was required (total 8.2 ml).

Calculated on the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid. ($C_6H_6O_5K_2$) requires 8.47 ml 0.1 N hydrochloric acid.

Methyl tropinonecarboxylate (IX, R = CH_3). Experiment 1. For the synthesis of the base and the hydrochloride 13.7 g dimethoxytetrahydrofuran (XIX, R = CH_3) was added (in one lot) to 116 ml 1 N hydrochloric acid, heated to 80° and the mixture was stirred at this temperature for 20 min. The reaction mixture was cooled rapidly to 0°, after which were added successively 88 ml 1 N hydrochloric acid, 38 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII), 106 ml of a 12% aqueous solution of sodium citrate and 10.9 g methylamine hydrochloride. The resulting mixture was stirred at 30° for 4 hrs.

The course of formation of the methyl tropinonecarboxylate (IX, R = CH_3) was followed by a gravimetric method, by determining it as the reineckate. For this purpose a 2 ml test portion of the reaction mixture was mixed with 25 ml of a 1% aqueous solution of Reinecke salt, acidified with hydrochloric acid (d^{20}_4 1.19) and brought to a volume of 50 ml with distilled water. The precipitate formed after 60 min was filtered off and dried in a vacuum desiccator. M. p. 156-158° (decomp.).

Found %: N 18.93, 18.80. $C_{14}H_{22}O_3N_7S_4Cr$. Calculated %: N 18.99.

The reaction mixture was cooled to 0°, saturated with 180 g potassium carbonate and extracted with benzene (4 times with 150 ml) by stirring for 10-15 min. The residue, after removal of the solvent, was redistilled. Yield 11.5 g (56.2% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). B. p. 85-88° (0.2 mm).

Found %: N 7.10, 6.95. $C_{10}H_{15}O_3N$. Calculated %: N 7.09.

Hydrochloride of methyl tropinonecarboxylate, m. p. 172-173°.

Found %: C 51.58, 51.39; H 7.06, 6.70; N 6.17, 6.13. $C_{10}H_{16}O_3NCl$. Calculated %: C 51.39; H 6.9; N 5.99.

Experiment 2. For the preparation of the hydrate of the base, 66 g dimethoxytetrahydrofuran (XIX, R = = CH_3) was added to 500 ml hydrochloric acid heated to 80° and stirred at that temperature for 20 min, after which the mixture was cooled rapidly to 10°. To the solution of succindialdehyde (VII) formed was added consecutively 484 ml 1 N hydrochloric acid, 165 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII), 49.5 g sodium acetate and 48.4 g methylamine hydrochloride, and the reaction mixture was stirred for 4 hrs at 29-31°. Then after cooling to 10° it was acidified to pH 4 with hydrochloric acid (d^{20}_4 1.19), extracted with 200 ml ether, saturated with 500 g potassium carbonate and finally extracted with 1000 ml benzene. After removal of the solvent in vacuo 79.2 g of a brown, oily residue was obtained, from which the methyl tropinonecarboxylate base (IX, R = CH_3) was isolated in the form of the hydrate . For this purpose 19.5 ml distilled water was added to the crude methyl tropinonecarboxylate (IX, R = CH_3). The mass rapidly solidified on trituration. The crystals formed were filtered off, washed with 75 ml absolute ether and recrystallized from methanol. Yield 68.4 g (56.1% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). M. p. 94-96°.

Found %: N 5.91, 5.82. $C_{10}H_{15}O_3N \cdot 2.5H_2O$. Calculated %: N 5.78.

Experiment 3. For preparing the base 15 g succindialdehyde ethyl diacetal (XIV) was stirred for 1 hr with 140 ml sulfuric acid (d^{20}_4 1.030) at room temperature. Then to the reaction mixture, cooled to −5°, was added consecutively a solution of 20 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylate, previously neutralized at 0°, 7.4 ml hydrochloric acid (d^{20}_4 1.19), 7.9 g sodium citrate and 6 g methylamine hydrochloride. The resulting mixture was stirred at 30° for 4 hrs, saturated at 0-5° with 150 g potassium carbonate and extracted with 600 ml benzene. The residue, weighing 10.1 g, crystallized out after the solvent had been distilled off in vacuo (20 mm). For purification it was recrystallized from methyl alcohol. Yield 7.45 g (59% calculated on the succindialdehyde ethyl diacetal (XIV)). M. p. 106-107°.

Found %: C 61.15, 61.10; H 7.44, 7.65. $C_{10}H_{15}O_3N$. Calculated %: C 60.89; H 7.66.

Experiment 4. For the synthesis of the hydrate and the free base, to a solution of 4.3 g succindialdehyde (VII) in 100 ml 1 N hydrochloric acid was added 18.9 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII) and 4 g sodium acetate or 50 ml of a 12% aqueous solution of sodium citrate (pH 4.5-5), after which 5.35 g methylamine hydrochloride was added. The solution obtained was stirred for 4 hrs at 30-31°. The reaction mixture was then cooled to 10°, saturated with potassium carbonate and extracted with 150 ml benzene. The solvent was distilled from the extract after drying over sodium sulfate and the methyl tropinonecarboxylate base (IX, R = CH_3) was isolated in the form of the hydrate. Yield 8.63 g (61.3%). M. p. 94-96°.

On drying in a vacuum desiccator over phosphorus pentoxide the hydrate lost water and was converted to the base (IX, R = CH_3). M. p. 106.4-107.6°.

Found %: C 60.78, 61.12; H 7.91, 7.65; N 7.14, 7.04. $C_{10}H_{15}O_3N$. Calculated %: C 60.89; H 7.66; N 7.09.

Tropinone (III). 114 g dimethoxytetrahydrofuran (XIX, R = CH_3) was added to 862 ml 1 N hydrochloric acid, heated to 80°, and stirred at this temperature for 20 min. 176 g acetonedicarboxylic acid (X) was then dissolved gradually in the reaction mixture after cooling the latter to 10°, after this the pH was brought to 5, at 5-10°, by means of potassium carbonate (about 195 g), and 900 ml of a 12% aqueous solution of sodium citrate and 81 g methylamine hydrochloride was added. The resulting mixture was stirred at 30°. The course of formation of tropinone (III) was followed by a gravimetric method by determining it as the reineckate [10] (see experiment 1). M. p. 180-182 (decomp.).

After 4 hrs the content of tropinone in the solution analyzed was 75% of theory, calculated on the dimethoxytetrahydrofuran (XIX, R = CH_3). The reaction mixture was then cooled to 0°, saturated with 750 g potassium carbonate and extracted with benzene (4 times with 900 ml). The residue after removal of the solvent was redistilled. Yield 67.9 g (56.56% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). B. p. 69-71° (4 mm), m. p. 41-42°.

Found %: C 69.05, 68.91; H 9.30, 9.18; N 9.82, 9.90. $C_8H_{13}ON$. Calculated %: C 69.03; H 9.41; N 10.06.

Tropine (I). Experiment 1. 29.7 g tropinone (III) was dissolved in 150 ml anhydrous methyl alcohol and hydrogenated in the presence of 4.5 g Raney nickel catalyst at room temperature and 60 atmos for a period of 4 hrs. The catalyst was filtered off and washed with 30 ml anhydrous methanol. The residue after removal of the solvent was redistilled. Yield 24.35 g (80.67%). B. p. 102-104° (7 mm).

Found %: C 68.13, 68.22; H 10.43, 10.58; N 10.10, 10.12. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.91.

Experiment 2. 20 g tropinone (III) was hydrogenated under the conditions of experiment 1. The residue after removal of methyl alcohol was dried by adding dry benzene and subsequent vacuum distillation (15-30 mm). The tropine obtained, weighing 19.2 g, was recrystallized from ether. Yield 16.4 g (80.84%). M. p. 61-62°.

Found %: C 67.89, 67.99; H 11.07, 10.92; N 9.66, 9.72. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.91.

A mixture of the synthetic tropine (m. p. 61-62°) with tropine (m. p. 59-61°) isolated from the natural alkaloid atropine gave no depression of the melting point.

SUMMARY

1. The spatially directed catalytic hydrogenation of tropinone to tropine has been achieved.

2. It has been established that depending on the reducing agent (reduction by sodium amalgam, electrolytically or by hydrogenation in the presence of Raney nickel catalyst, or platinum or palladium oxide) and on the reaction conditions the tropane-3-ols are obtained with varying relative contents of steric isomers.

3. Methods of preparing esters of tropinecarboxylic acid have been studied.

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Received April 18, 1957

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REACTIONS OF MAGNESYLAMINES

V. THE MECHANISM OF THE REACTION OF ARYL AMIDATION OF AROMATIC ALDEHYDES BY N,N-BIS-(MAGNESIUM HALIDE)-ARYL AMINES

P. A. Petiunin and L. A. Tetiueva

To explain the mechanism of the reaction of aryl amidation of aromatic aldehydes by N,N-bis-(magnesium halide)-aryl amines it was first necessary to study the ratio of magnesylamines to aldehydes, since this question has not been considered in the literature. The first experiments were carried out with monomagnesylamines. They showed that phenylbromomagnesylamine (I) reacts energetically with benzaldehyde, but after decomposition of the reaction mass there was separation again into aniline and benzaldehyde, and only small amounts of benzanilide were formed. We could assign to the magnesium organic complex (II) formed by the reaction of (I) with benzaldehyde the structure of a bromomagnesium alcoholate of a hydroxyamine.

$$\underset{(I)}{C_6H_5NHMgBr} + C_6H_5CHO \rightarrow \underset{(II)}{C_6H_5CH(OMgBr)NHC_6H_5}$$

The halogenomagnesium alcoholate nature of this complex well explains the hydrolysis to form aniline and benzaldehyde and also its inability to react with ethyl benzoate (experiment 2a). Along with these experiments it was shown that monomagnesylamines in general, and also the magnesium organic complex (II) (experiment 2b), cannot catalyze the reaction of aryl amidation of aldehydes.

The small amount of benzanilide which we did succeed in obtaining in the previous experiment evidently came from the presence of dimagnesylamine in the reagent. The latter can be formed along with (I) in the reaction between aniline and ethylmagnesiumbromide.

The assumption that monomagnesylamine cannot catalyze the reaction of aryl amidation of aldehydes also was confirmed experimentally in the reaction with N-ethylaniline. Ethylaniline gives with ethylmagnesiumbromide only monomagnesium derivatives which in the experiment with benzaldehyde give no N-ethylanilide of benzoic acid.

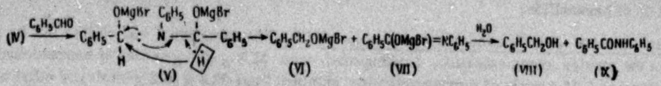
Further studies were carried out toward explaining the role of dimagnesylamines in the aryl amidation of aldehydes. Thus, when equivalent amounts of N,N,-bis-(bromomagnesium)-aniline (III) react with benzaldehyde, the yield of benzanilide rises to 3%. The reaction occurs by the following scheme:

$$\underset{(III)}{C_6H_5N(MgBr)_2} + C_6H_5CHO \rightarrow \underset{(IV)}{C_6H_5CH(OMgBr)N(MgBr)C_6H_5}$$

The magnesium organic complex (IV) thus formed has both a halogenomagnesium alcoholate and a halogenomagnesylamine character. On hydrolysis it splits into aniline and benzaldehyde. As a halogenomagnesylamine derivative it reacts with ethyl benzoate.

We note that when we turn from the experiment with monomagnesylamine to the experiment with dimagnesylamine, the yield of benzanilide rises from 1 to 3%, that is, 3 times. This is direct evidence that aryl amidation of the aldehyde goes only through the dimagnesylamine.

Earlier [1] it was shown that the most successful aryl amidation occurs when 1 mole of dimagnesylamine reacts with 2 moles of benzaldehyde. Due to its halogenomagnesylamine character, complex (IV) can react with a new molecule of aldehyde* to form the halgoenomagnesium alcoholate of a dihydroxyamine (V), in which also an oxidation-reduction reaction occurs.



$$(IV) \xrightarrow{C_6H_5CHO} C_6H_5-\overset{OMgBr}{\underset{H}{C}}:\overset{C_6H_5}{N}-\overset{OMgBr}{C}-C_6H_5 \rightarrow C_6H_5CH_2OMgBr + C_6H_5C(OMgBr)=NC_6H_5 \xrightarrow{H_2O} C_6H_5CH_2OH + C_6H_5CONHC_6H_5$$

(V) (VI) (VII) (VIII) (IX)

The thus formed halogenomagnesium alcoholate of benzyl alcohol (VI) and the magnesium halide derivative of the lactim form of benzaldehyde (VII) are further decomposed into the alcohol (VIII) and benzanilide (IX).

In our work [1] the aryl amidation of aldehydes with N,N-bis-(halogenomagnesium)-arylamines was assigned to the type of oxidation-reduction reactions although only aryl amides were isolated from the final reaction product. In the present work in special experiments we have isolated and identified a second end product of the reaction, benzyl alcohol (experiment 6). Thus, our assumption as to the oxidation-reduction nature of this reaction has been confirmed experimentally. Just as in the case of the Cannizzaro reaction [2] we can probably admit that in complex (V) splitting of the bond occurs homolytically. Hence, in an oxidative-reductive transformation of complex (V), the boiling point and chemical nature of the solvent in which the reaction is carried out should have great influence.

EXPERIMENTAL

1. Reaction of phenylbromomagnesylamine (I) with benzaldehyde in the ratio 1:1. To 0.05 g-mole of ethylmagnesium bromide obtained in the usual way from 5.45 g ethyl bromide and 1.2 g magnesium in 30 ml of ether was added with good cooling and stirring a solution of 4.66 g (0.05 g-mole) of aniline in 15 ml of ether. To the resulting (I) was added a solution of 5.3 g (0.05 g-mole) of benzaldehyde in 20 ml of ether. Energetic boiling occurred. The contents of the flask were heated for 2 hrs on the water bath and the magnesium organic complex (II) was decomposed with dilute hydrochloric acid. The ether layer was separated and the ether and also the unreacted benzaldehyde were distilled off with steam. In the distillation flask there remained 0.1 g of benzanilide (1% calculated on the aniline taken in the reaction). Needles from toluene, m. p. 163° [3]. Aniline was isolated in the usual way from the aqueous acid layer.

2. Reaction of the magnesium organic complex (II) with ethyl benzoate and benzaldehyde. a) The magnesium organic complex (II) obtained by the method of the previous experiment was treated with 3.75 g (0.025 g-mole) of ethyl benzoate in 15 ml of ether (boiling of the ether did not occur). The reaction mass was heated 2 hrs on the water bath, decomposed with dilute hydrochloric acid, and treated further as in experiment 1. Yield of benzanilide 0.1 g (1%).

b) The reaction between (II) and benzaldehyde in equimolar quantities was carried out in exactly the same way. The ether did not boil when the benzaldehyde was added. After decomposition of the reaction mass we isolated benzaldehyde, aniline, and 1% benzanilide.

3. Reaction of phenylethylbromomagnesylamine with benzaldehyde in the ratio 1:1. To 0.05 g-mole of ethyl bromide was added 6.05 g (0.05 g-mole) of N-ethylaniline in 20 ml of ether and the mixture was heated for 30 min on the water bath. Then we added 5.03 g (0.05 g-mole) of benzaldehyde in 20 ml of ether; boiling of the ether occurred. In conclusion the reaction mass was heated 2 hours on the water bath, decomposed by dilute hydrochloric acid, and treated further as in experiment 1. As a result, we isolated benzaldehyde and ethylaniline. Formation of the N-ethylanilide of benzoic acid was not observed.

4. Reaction of N,N-bis-(bromomagnesium)-aniline (III) with benzaldehyde in 1:1 ratio. To 0.05 g-mole of N,N-bis-(bromomagnesium)-aniline, obtained by the method of [4], with good cooling and stirring we slowly added a solution of 6.05 g (0.05 g-mole) of benzaldehyde in 20 ml of ether. The contents of the flask were heated 2 hrs on the water bath and the magnesium organic complex (IV) was decomposed with dilute hydrochloric acid and then treated as in experiment 1. We obtained 0.3 g of benzanilide (3%).

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* Experiments describing the reaction between dimagnesylamines and aldehydes in the ratio 1:2 were published in the previous communication.

5. Course of the reaction between the magnesium organic complex (IV) and ethyl benzoate. The magnesium organic complex (IV) obtained by the method of the previous experiment was treated with a solution of 3.75 g (0.025 g-mole) of ethyl benzoate in 20 ml of ether. Energetic boiling of the ether occurred. In conclusion the reaction mass was heated for 2 hrs on the water bath and then treated as in the previous experiments. Yield 1.2 g (12.2 %) of benzanilide.

6. Isolation and identification of benzyl alcohol (VIII). The experiment was carried out by process B, described in the previous communication. Starting substances: 31.8 g (0.3 g-mole) of benzaldehyde in 60 ml of dry pyridine and 0.15 g-mole of dimagnesylamine, obtained from 32.4 g (0.3 g-mole) of ethyl bromide. 7.2 g (0.3 g-mole) magnesium, and 13.8 g (0.15 g-mole) of aniline. The reaction mass was decomposed with dilute hydrochloric acid and the benzanilide which separated was filtered and washed with ether. Yield 11.3 g (38.3% calculated on the aniline taken for the reaction). The filtrate was extracted three times with ether, the ether extracts were combined and most of the ether was distilled off. For separation of the unreacted benzaldehyde the residue was shaken 4 times with a 40% solution of sodium bisulfite, 10 ml each time. Then the ether layer was shaken with a solution of sodium bicarbonate (to remove the dissolved sulfurous acid) and dried over sodium sulfate. After removal of the solvent, the residue was distilled at atmospheric pressure and the fraction boiling 201-205° was collected. Yield, 7.1 g (21.9% calculated on the benzaldehyde taken for the reaction). Benzyl alcohol was identified by reaction with hydrobromic acid (formation of benzyl bromide) and by reaction with phenyl isocyanate. The phenylurethane melted at 77-78°. The literature records 78° [5]. A mixed melting point with known phenylurethane showed no depression.

SUMMARY

We have assumed and experimentally established the mechanism of the reaction of aryl amidation of aromatic aldehydes by N,N-bis-(halogenomagnesium)-aryl amines.

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Received January 27, 1957

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THE OCCURRENCE OF EQUILIBRIUM OF THREE LIQUID PHASES IN TERNARY SYSTEMS

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Until recently stable equilibrium of three liquid phases has been found in ternary systems formed by binary systems with stable phase separation. It has also been shown [1] that equilibrium of three liquid phases can occur in ternary systems which contain a binary system with metastable phase separation. In the case studied, the three-phase liquid equilibrium was also metastable and occurred according to the same scheme as the stable phase separation. Stable equilibrium of three liquid phases in a ternary system containing one or several binary systems with metastable phase separation has not been studied. The study of this type of equilibrium and the method of its formation is the purpose of the present work.

EXPERIMENTAL

We selected for the study of this question the ternary system anthranilic acid—water—benzine. The binary system anthranilic acid—benzine was studied in this work to relate it to systems with metastable phase separation. The system water—benzine belongs to systems with stable phase separation and a very high upper critical point [1]. The system water—anthranilic acid has been studied for stratification [2]. The curve for the metastable phase separation of the system has an upper critical point at 78°, corresponding to 38% anthranilic acid. Thus, the chosen ternary system contains two binary systems with metastable phase separation and one with stable separation.

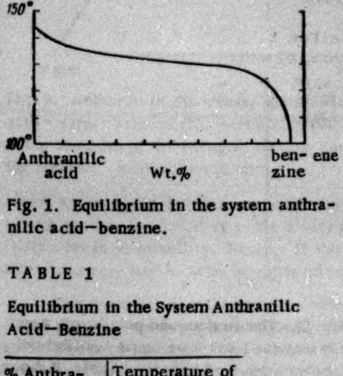

Fig. 1. Equilibrium in the system anthranilic acid—benzine.

TABLE 1

Equilibrium in the System Anthranilic Acid—Benzine

% Anthranilic acid	Temperature of crystallization
5.00	107.0°
20.00	127.0
40.00	130.0
60.00	132.5
80.00	134.5
100.00	145.0

We used the following reagents in the study: C. P. anthranilic acid, m. p. 145°, twice distilled water, and a benzine fraction boiling in the range 90-120°. Equilibrium between two and three liquid phases was studied by the visual-polythermal method of V. F. Alekseev [3] in a sealed glass ampule in an oil thermostat. In the same ampule and thermostat we also studied crystallization in the system anthranilic acid—benzine using an inner heater [4].

The system anthranilic acid—benzine was studied by fusibility (Table 1 and Fig. 1). As Fig. 1 shows, the curve of crystallization of anthranilic acid has a very sloping S-shape and occupies almost all the concentration intervals of the system. Such a form for the crystallization curve should indicate the presence under it of a curve of metastable phase separation. The latter is found at very low temperatures, since experimentally it was not observed with supercooling. Its presence could be shown indirectly, as will be demonstrated below.

The ternary system anthranilic acid—water—benzine was studied by stratification. We studied six polythermal sections through its temperature-concentration prism, going from its anthranilic acid

TABLE 2

Polytherms of the System Anthranilic Acid—Water—Benzine

% Anthranilic acid	Temperature		% Anthranilic acid	Temperature	
	2-phase stratification	3-phase stratification		2-phase stratification	3-phase stratification
Section 1			Section 2		
5% benzine, 95% water			20% benzine, 80% water		
49.00	70.0°	—	40.00	—	98.0°
49.50	91.0	—	45.00	—	101.0
50.00	115.0	—	50.00	—	110.0
			55.00	—	116.5
			60.00	—	121.5
			65.00	—	123.5
			70.00	—	121.0
			72.00	—	118.0
			78.00	122.0°	—
			79.00	105.0	—
			79.50	95.0	—
Section 3			Section 4		
40% benzine, 60% water			60% benzine, 40% water		
35.00	—	97.0°	35.00	—	95.0°
40.00	—	104.0	40.00	—	106.0
45.00	—	110.0	45.00	—	114.0
50.00	—	116.0	50.00	—	120.0
55.00	—	120.0	55.00	—	123.5
60.00	—	123.0	60.00	—	121.0
65.00	—	124.0	65.00	—	117.0
70.00	—	119.0	70.00	—	112.0
75.00	—	112.0	75.00	—	105.0
80.00	—	105.0	76.00	—	99.0
81.00	—	100.0	84.00	120.0°	—
85.00	119.0°	—	85.00	102.0	—
85.50	108.0	—	85.50	88.0	—
86.00	94.0	—			
Section 5			Section 6		
80% benzine, 20% water			98% benzine, 2% water		
35.00	—	100.0°	50.00	93.0°	—
40.00	—	108.0	60.00	109.0	—
45.00	—	115.0	70.00	120.0	—
50.00	—	121.0			
55.00	—	123.5			
60.00	—	115.0			
62.00	—	109.0			
63.00	—	98.0			
80.00	119.0°	—			
82.00	103.0	—			
84.00	90.0	—			

edge to the boundary of the binary system water—benzine (Table 2, Fig. 2). The sections and polytherms were numbered in the order of increasing benzine content in the mixture. In sections 1 and 6 we found equilibrium only between the two liquid phases, in the others, between two and between three liquid phases. As Fig. 2 shows, the polytherm of the two-phase liquid is almost a vertical line. Thus, the reciprocal solubility of the two-liquid phases in the ternary system depends little on temperature. Between these polytherms and the anthranilic acid edge lies a field of unsaturated homogeneous solutions. Between them and the boundary of the system benzine—water lies a field of heterogeneous liquid solutions. The polytherms of the three-phase liquid state are curves with maxima at about the same temperature, 124°. This corresponds to their location on the critical conode of the three-phase liquid equilibrium.

From the experimentally obtained polytherms we constructed the isothermal sections of the prisms of the ternary system anthranilic acid—water—benzine at 100, 110, and 120°. A projection isotherm is shown on the

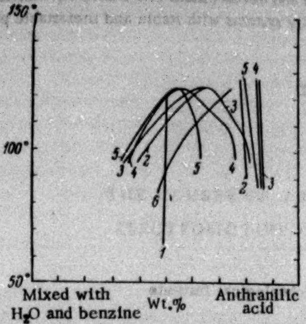

Fig. 2. Polytherms of the ternary system anthranilic acid—water—benzine. Explanation in text.

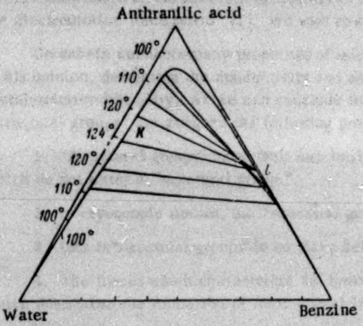

Fig. 3. Isotherms of the ternary system anthranilic acid—water—benzine (KL — critical conode; figures along the sides of the triangle relate to the corresponding conode). Explanation in text.

triangle in Fig. 3, on which is shown the projection of the critical conode KL of the three-phase liquid state. On Fig. 3 the curve of the two-phase liquid state is shown at 100° only; the other two almost agree with it since the liquid phase equilibrium is practically unchanged with temperature. The field of the two-phase liquid state which adjoins the triangle of the three-liquid phases on the side of the binary system anthranilic acid—water is very narrow. Therefore, it was not determined.

In the ternary system anthranilic acid—water—benzine the following processes occur as the temperature is lowered. In the stable state at high temperature, phase separation of the binary system water—benzine is homogenized by anthranilic acid. The content of the latter in the heterogeneous mixture reaches 86%. The system anthranilic acid—water is dominant among the binary systems of the ternary system. At 124° there appears on the binodal curve the critical solution K (composition 67% anthranilic acid, 29.5% water, and 3.5% benzine) and the corresponding solution L (46% anthranilic acid, 1% water, and 53% benzine), and the critical conode KL is formed. When the temperature is lowered the volume of three-phase liquid state develops from the latter. On the isotherm appears the triangular equilibrium of three liquid phases from the side of which to the side of the binary homogeneous system there develops a field of a two-phase liquid equilibrium. In the metastable state at 78° one of the equilibrium fields of two-liquid phases of the ternary systemreached the field of binary system anthranilic acid—water. A shift then occurs in the dominant system. The binary system anthranilic acid—benzine becomes dominant. This confirms the idea established earlier that in ternary systems with an equilibrium of three liquid phases the temperature at which the dominating systems change is the critical solution temperature of that binary system which lies between the other two binary systems. As that temperature is lowered further, a third field of a two-phase liquid state of the ternary system reaches the boundary of the binary system anthranilic acid—benzine. In the latter from this moment appears a break in solubility. Because of this the binary system anthranilic acid—benzine must be considered a system with a very low location of upper critical point.

The processes described are analogous to those which occur in the formation of a stable equilibrium of three liquid phases in ternary systems which contain binary systems with stable phase separation. Thus, the polythermal scheme of occurrence and development of stable three phase liquid equilibrium is the same in ternary systems which contain binary systems with stable and metastable phase separation.

SUMMARY

1. We have studied the binary system anthranilic acid—benzine by the fusibility method. We have shown that it belongs to systems with metastable phase separation with a very low position for the upper critical point.

2. We have studied phase separation in the ternary system anthranilic acid—water—benzine. We have found in it a volume of a stable equilibrium of three liquid phases at temperatures below 124° (the critical temperature of the conode). We have found the temperature-concentration boundaries of the area of the three-phase liquid equilibrium and the composition of the corresponding solutions of the critical conode.

3. We have shown that the polythermal scheme of occurrence and development of a stable equilibrium of three liquid phases is the same in ternary systems which contain binary systems with stable and metastable phase separation.

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Received March 18, 1957

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* Original Russian pagination. See C. B. translation.

THE CAUSES OF THE TRANSPOSITION OF METALS IN THE ELECTROMOTIVE FORCE SERIES IN FUSED ELECTROLYTES

Iu. K. Delimarskii

Recently, E. Ia. Gorenbein [1, 2] has considered the question of the causes for the transposition of metals in the electromotive force series. This author has concluded one of his papers as follows. "On the basis of the present knowledge of the structure of liquids, an explanation is given for the causes of transposition of metals in the electromotive force series" [1]. We wish to make some comments on this explanation.

Gorenbein connects many properties of solutions and melts with the formation of "structural groups" which, in his opinion, determine the conductivity and osmotic pressure of solutions, and also assure equilibrium at the metal-solution boundary. As we can conclude from a series of papers by Gorenbein [1-5], these hypothetical "structural groups" are assigned the following properties by him.

1. "Structural groups" have their own intrinsic conductivity, higher than the conductivity of the same ions which do not enter a "structural group."

2. In cryoscopic studies, the "structural groups" behave as separate kinetic particles.

3. Ions in "structural groups" do not have definite potentials.

4. The forces which characterize the formation of "structural groups" are of the same nature as the forces which determine the formation of ionic crystal lattices.

It is a matter of primary interest to determine how far these views of Gorenbein can be considered to be scientifically established and how they relate to the transposition of metals in the electrochemical series.

As is known, the idea of the quasi-crystalline structure of liquids was introduced by Stewart [6, 7] who showed experimentally (roentgenographically) that liquids near the melting point often keep a crystalline structure. Stewart also brought about an understanding of the regularities which he called "cybotactic groups." The quasi-crystalline arrangement of liquids was also experimentally established by Danilov [8], Donat [9], and other authors. At the present time this arrangement of liquids is accepted as being present in areas in which the molecular distributions are similar to but not identical with the crystalline state [10]. Such ideas come chiefly from Frenkel [11] and Danilov [12] who have successfully developed these ideas. The latter especially has shown that quasi-crystalline structures are also found in solutions. At the present time the theory of the quasi-crystalline structure of solutions has been developed by many workers [10, 13-18]. The basic ideas of this theory are the following.

1. In solutions there is a close arrangement and a quasi-crystalline distribution of molecules.

2. In solutions a fluctuation of concentration occurs which differentiates solutions from pure liquids [14].

3. The number of most closely adjacent molecules is determined by a coordination number which is characteristic of the structure of the solution.

4. Reaction between molecules which make up the solution is produced by their general momentum and the distance between them [10].

5. In solution there occur processes of solvation and association which can be considered as intermediate steps in the formation of chemical compounds. Solvation and association either alter the quasi-crystalline structure of the solvent or form a new quasi-crystalline structure with it.

These theoretical ideas are based on experimental data: roentgenographic, optical (light dispersion), thermochemical (calorimetric), and others. It is not hard to see that in the quasi-crystalline theory of solutions there is no place for "structural groups" with properties such as those described by Gorenbein. The structural groups of Gorenbein do not fluctuate and there is no quasi-crystalline formation of a close arrangement for this is not an independent kinetic particle which can change the osmotic pressure. His groups are not associations, for these do not have their own superconductivity. In no case has this been shown. What, then, are the "structural groups" of Gorenbein? We consider what he himself has written. We read the following concerning the intrinsic conductivity of the "structural groups": "We explain the increased corrected molecular conductivity with increased concentration by the rise in the number of structural groups which have their own conductivity. Ions can migrate not only into the structural groups, but also can transfer from one group to another. It seems to us that the conductivity of the structural groups can be compared to the mechanism of conductivity in crystals, with this difference, that in structural groups both cations and anions take part in the transmission of the current" [5].

If the intrinsic conductivity of the "structural groups" is compared to the conductivity of the ions of a crystal, as Gorenbein says, then the statement that the structural groups should be higher than that of the same ions which are not in structural groups contradicts the present theory of the conductivity of the ions of crystals. According to the theory of Frenkel [19], not all the ions share in the conductivity, but only those which under the influence of thermal motion have been torn from their positions, or are so "activated" that they can easily be torn from them. Thus, the greater the defects in the crystal lattice and the more the "free" ions, the higher will be the conductivity. With increase in temperature, there is an increase in the number of "activated" ions and the conductivity rises. As is known, Frenkel has assumed a temperature relation of conductivity for the ions of crystals of

$$\varkappa = A \cdot e^{-\frac{u}{kT}} \tag{1}$$

Much experimental data on the conductivity of fused salts has shown the correctness of Eq. (1) for them.

Thus we can say that the mechanisms of the conductivity for the ions of crystals and the ions of melts have much in common. If this is so, then it is quite impossible to assert that ions combined in "structural groups" will migrate faster in an electrical field than do "free ions." This clearly contradicts the assumption of Gorenbein of the presence of some sort of structural group which would have a higher conductivity than systems which consist of the same "free" ions.

There is no clarity in the idea of Gorenbein on "structural groups" as independent kinetic particles. On this question Gorenbein writes, "These structural groups in cryoscopic studies behave as separate kinetic particles" [2]. As already mentioned, the existence of these "structural groups" as free kinetic particles does not come from the quasi-crystalline theory of the structure of solutions. In one of his papers, Gorenbein [1] calls his "structural groups" associates. By associates we mean molecular compounds formed from one type of molecules. If "structural groups" are such associates, then why say that he has worked out a new theory of concentrated solutions as if based on the present theory of the liquid state.

Any theory of solutions must establish a theoretical basis for the relation of thermodynamic properties to the concentration of the components. This important element is absent from the discussions of Gorenbein. Following Sakhanov [20, 21] he introduces a correction for the conductivity with viscosity but gives only

$$\varkappa_{\text{corr.}} = \varphi(c), \tag{2}$$

where χ_{corr} is the specific conductivity corrected for viscosity. The empirically established form of this function cannot be considered as a new theory of solutions. As was very truly shown by Izmailov [22], such an unconditional correction of conductivity for viscosity cannot be considered proper.

When Gorenbein turns to a consideration of the results of a potentiometric measurement, his "structural groups" acquire new properties. They lose their kinetic mobility and the ions which enter the structural groups and which migrated so strongly in the conductivity measurements, now "do not wish" to exchange with the atoms on the surface of the metal electrode, that is, do not share in transfer of current. Such contradictory properties of the "structural groups" are probably explained by the fact that they exist only as theoretical constructions of Gorenbein. As shown above, ideas of "structural groups" with such properties as Gorenbein ascribes to them are contradictory to the theory of the quasi-crystalline structure of solutions and also to the theory of conductivity of ions of crystals and melts.

In one paper [1] Gorenbein attempts to show that the transposition of metals in the electrochemical series occurs chiefly in solutions with a low dielectric permeability (DP). However, this is not so. It is well known that the electrochemical series is changed in a series of individual salts with common anions and also in solvents with a high DP, for example, in fused salts (NaF, NaCl$-$KCl$-$SrCl$_2$, NaBr$-$KBr, NaI and others) [23]. Gorenbein groundlessly considers aluminum halides as dielectrics which enter the composition of such fused systems, in which their content does not exceed 50 mole%. It is well known that aluminum halides form strong complexes with the halides of other metals [24-26]. Such compounds as KAlCl$_4$ are so stable that they form even in the vapor [27]. Therefore, for example, in systems KCl$-$AlCl$_3$ or KBr$-$AlBr$_3$ to consider AlCl$_3$ or AlBr$_3$ as dielectrics is as impossible as to consider SO$_3$ a dielectric in the compound K$_2$SO$_4$.

Gorenbein is forced to consider low DP and fused systems which contain aluminum halides in this way so as to account for the formation of his "structural groups" in fused salts. However, as shown above, the idea of "structural groups" (as understood by Gorenbein) does not help at all to solve the problem of the concentration of the potential determining ions in a fusion. An explanation for the reason for the transposition of metals in the electromotive force series on the basis of an assumption of the presence in the melt of associates and complexes, shown by different experimental methods, is undoubtedly more reasonable than the use of the "structural groups" assumed by Gorenbein. Among other things, the statement of Gorenbein [1] that investigators have not turned their attention to the possibility of formation of cation complexes in solutions and melts is based on a misunderstanding. Sufficient acquaintance with the review paper of L. N. Antipin [28] would convince him of the contrary. In particular, for the aluminum halides, for which Gorenbein does not recognize cation complexes, the formation of these is possible according to the scheme: $2AlCl_3 \rightleftharpoons AlCl_2^+ + AlCl_4^-$.

For an explanation of some regular changes in the value of the electrode potential in fused salts aside from complex formation, we were attracted to the idea of reciprocal polarization of the ions of the melt and of atom-anion polarization on the surface of the electrode.

In one of his papers [2], Gorenbein tries to connect reciprocal polarizability of ions with the formation of "structural groups." In relation to this question we read the following: "It is known that the polarizability of halogen ions increases from the fluorine ion to the iodine ion. Therefore, the degree of regulation with other conditions equal will be greater for electrolytes with iodine anions. For such solutions the concentration of the potential determining ion will be less; therefore, the corresponding value of the electrode potential is changed, as is actually found." Then follows a reference to a work [29] which reports the results of an experimental study of the potential of decomposition of some metal halides in SnCl$_2$ and SnBr$_2$ as solvents. This work [29] shows that in these solvents the electrochemical series is somewhat different. However, Izbekov and Skobets [29] did not study fluorides or iodides and also did not determine the values for the electrode potentials in fluroides, chlorides, bromides, and iodides. Therefore, the data of these authors can in no way confirm the ideas expressed above by Gorenbein.

Cation	Equivalent conductivity at the melting point			
	anion			
	F^-	Cl^-	Br^-	I^-
Na^+	77.2	133.5	132.0	134.0
K^+	95.5	104.0	124.0	89.0
Ag^+	—	124.2	104.2	85.8
Tl^+	—	46.6	31.7	24.8
Cd^{2+}	—	51.8	32.0	6.4
In^{3+}	—	14.7	6.4	2.3

In connecting polarizability of ions with regulation, Gorenbein once more contradicts himself. As was noted above, according to Gorenbein, conductivity will be higher, the greater the regularity. If, as Gorenbein writes [2], regularity rises in the order fluoride, chloride, bromide, iodide, then the conductivity should rise in the same order. As to how this assumption of Gorenbein agrees with the observed facts is clear from the data on conductivity given in the table.

For the heavy metal halides the conductivity, in spite of Gorenbein, regularly decreases as we go from chlorides to iodides. As to the alkali metal halides, it is difficult to speak of a regular change in conductivity.

According to Gorenbein, the maximum concentration of the potential determining ion should be found for fluorides. Therefore, in fusions of fluorides the electrode potential of metals, it would seem, should be more positive than for the other halides. However, experiment does not confirm this. The electrode potential in fusion of fluorides is more negative than in fusions of iodides [30]. This fact is satisfactorily explained by assuming a reciprocal polarization of the ions and is in sharp contradiction to the ideas of Gorenbein. We find it necessary to remark that the explanation of the transposition of metals in the electromotive force series on the basis of ideas of "structural groups" developed by Gorenbein contradicts a very considerable number of facts.

Thus, the explanation of Gorenbein of the causes of transposition of metals in the electromotive force series in fused salts is implausible in all its assumptions of "structural groups" with their astonishing properties.

SUMMARY

1. The idea of the existence in solutions and fusions of special "structural groups' which have an intrinsic conductivity greater than that of the free ions which compose them, in spite of the statements of E. Ia. Gorenbein, is not derived from the quasi-crystalline theory of liquids and contradicts the present theory of conductivity.

2. The attempts of E. Ia. Gorenbein to explain by his "structural groups" the reason for the transposition of metals in the electromotive force series (for fused electrolytes) are implausible and lead to contradiction of a large number of experimental facts.

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Received March 5, 1957

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IN MEMORY OF ANDREI IVANOVICH LUN'IAK

On October 15, 1957 in his 76th year, after a heavy and prolonged illness, Andrei Ivanovich Lun'iak died; he was professor of chemistry in the Kazan Medical Institute, a pupil of A. M. Zaitsev.

A. I. Lun'iak was born in St. Petersburg on December 17, 1881. He finished the Odessa Gymnasium in the autumn of 1899 and entered the St. Petersburg Military Medical Academy. From the beginning of his training at the Academy, Lun'iak showed great interest in chemistry, a course which was taught by Prof. A. P. Dianin, under whose instruction Lun'iak made practical experiments in carrying out the different laboratory studies; while still a student in 1903 he completed a scientific study "On the Products of Condensation of Aliphatic Aldehydes with Phenol." This work was presented at a meeting of the Russian Chemical Society, and the Conference of the Military Medical Academy awarded it the Zinin Prize.

When he finished the Military Medical Academy in 1904, A. I. Lun'iak was appointed military physician in Kazan. However, he followed his inclinations and in his free time he continued to occupy himself with chemistry in the laboratory of Prof. A. M. Zaitsev. Later, in 1906, Lun'iak resigned from military service and devoted himself entirely to chemistry, becoming a student in the organic chemistry laboratory of Kazan University. Here, under the direction of A. M. Zaitsev, Lun'iak undertook the synthesis of high molecular weight tertiary alcohols by the action of acid anhydrides with alkyl halides in the presence of zinc and magnesium. At the same time he prepared, at the request of the university and by special permission, to take his Master's examination.

In the spring of 1908, on the recommendation of the Physicomathematical Faculty of the University, Lun'iak was sent for 2 years to Berlin, where he worked in the laboratory of E. Fischer on the synthesis of the dipeptide prolylphenylalanine and its optical isomers. The synthetic dipeptide was identified with the natural one obtained by the hydrolysis of a protein.

When he returned from abroad in 1910, A. I. Lun'iak was appointed privat-docent at Kazan University, where he continued to work on the problems of A. M. Zaitsev and taught a number of courses in the Physicomathematical and Medical Faculties.

In 1912 A. I. Lun'iak was chosen in a competition as adjunct professor in the chair of organic chemistry and agricultural analysis at the Novo-Aleksandrii Agricultural Institute. Here Lun'iak finished his Master's dissertation on the theme "The Action of Organic Zinc Halides on the Anhydrides of Monobasic Acids," which he defended in March, 1914 at Kiev University.

From 1916 to 1924 A. I. Lun'iak was professor of physiological chemistry in the newly opened Perm University where besides his teaching and research he turned to administrative and organizational activities. He was Dean of the Physicomathematical and Medical Faculties and then served as Rector of the University.

In 1924 A. I. Lun'iak was chosen by competition as professor of technical chemistry at Kazan University and at the same time gave a course in chemical technology in the Institute of Agriculture and Forestry. In 1925 he was chosen Rector of this Institute, and in 1926 Rector of the V. I. Ul'ianov-Lenin Kazan University.

From 1930 A. I. Lun'iak occupied the chair of organic chemistry in the Technological Faculty of the Kazan Chemicotechnological Institute, which was organized in the chemical division of the university. At the same time, with great energy A. I. Lun'iak worked on problems of technology and in 1929 took an active part in organizing a special higher technical school for fats in the Vahkitov Combine. At the same time, for many years, Lun'iak also taught organic chemistry.

In 1936 A. I. Lun'iak was chosen director of the chair of organic chemistry in the Kazan Medical Institute, where he taught chemistry for many years. In 1952 the state of his health forced him to retire but he did not lose interest in the work of the chair and he continued a lively interest in the life of the Institute.

Since he had great organizing ability and inexhaustible energy, Lun'iak knew how to introduce into any subject which he directed a stream of fresh initiative and lively ideas. In 1929 he was one of the active organizers of the 5th Mendeleev Congress which was successfully conducted in Kazan.

A. I. Lun'iak took an active part in the development of chemical industry of the Tartar Republic. The Party and the authorities valued his services highly and awarded him the Order of Lenin and a medal "For his great services in the War of 1941-1945."

The memory of A. I. Lun'iak will always remain in the hearts of his students and co-workers.

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7. Deriwate des L-Prolins und des Phenil-alanins
8. The Construction of a Cement-Fertilizer Combine in the Tartar Republic, Kazan Scientific and Economic Institute (Tatizdat, 1930) (with Prof. Bogorodskii and Engineer Sobolev).
9. Prospects for the Chemical Industry in the Tartar Area (Tatizdat, 1932) (with M. A. Iagudin and S. Ia. Arbatov).

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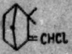
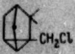
LETTER TO THE EDITOR

G. Chiurdoglu, Ch. Goldenberg, and J. Geeraerts

Recently [1] we reported that in the chlorination of camphene besides chlorides (I) and (II) there was formed the chloride (IV) and not (III) as stated by D. V. Tischenko [2].


(I)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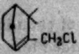
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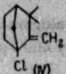
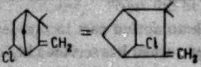

(IV)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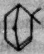
(VI)

The chloride which is the subject of the dispute certainly contains the semicyclic double bond $>C=CH_2$: $\nu_{C=C}$ 1647 cm^{-1}, δ 897 cm^{-1}, 2δ 1780 cm^{-1} (infrared spectrum).

This fact at one prevents accepting structure (III)* in accord with the Bredt rule [3], for which, since the work of Prelog [4], the limits of application ($1 \leq n \geq 5$) have become known for bridged compounds.

Speaking more accurately, we can say that with double bonds of the type $>C=CH_2$ two compounds (IV) and (V) are possible, both with relatively active chlorine.** We choose chloride (IV) because this substance gives an infrared spectrum identical with the spectrum of α-chlorocamphene, which we have prepared by the method of Meerwein [5].***

The purpose of our work has thus been attained, and we did not try either the synthesis or study of the alcohol ("camphenol") which is formed from this chloride, very possibly, as a result of the Wagner-Meerwein rearrangement.

The fact that Tishchenko obtained a compound $C_{10}H_{16}O_3$, not yet studied, by the oxidation of "camphenol" and not $C_9H_{14}O_2$, did not surprise us at all after the work of Maquestiau [7] which showed that camphene and its analogs like longifolene can be oxidized and are oxidized without loss of a carbon atom.

We assumed however, that our colleague would send us the "camphenol" and the product $C_{10}H_{16}O_3$ so that we could study its structure in our laboratory in Brussels. He told us that he had no more of these two substances.

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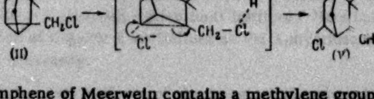
* Chloride (III) is, among other things, a derivative of camphenylene (VI) (mentioned by Snitter [6]) the impossibility of whose existence has been shown in various ways [7].

** According to present views [8] in a molecule like (V) chlorine activates the double bond because it separates the minimum distance. Compound (V) can be obtained in the following way:



*** The fact that 1-chlorocamphene of Meerwein contains a methylene group united by a double bond can serve, if it is necessary, as a confirmation of its structure.

Discussing the transformation of 1-chlorocamphene (IV) into 1-acetoxycamphene, D. V. Tishchenko considers that this transformation is impossible, since the corresponding carbonium ion should be flat.

The mechanism of the hydrolysis of chloride (IV) is a complex problem. If we assume that the reaction goes by the mechanism $S_N 1$, there should certainly be considerable strain in the cation of the intermediate stage. But if we doubt the possibility of existence of such an unstable intermediate condition with a very short life, then we should all the more exclude any possibility of the existence of a compound of the type of camphenylene (III), (VI), which would contain six coplanar atoms in the field of the double bonds. Finally, as to the last remark, we remind D. V. Tishchenko, that without the help of the spectroscope it would have been impossible in recent years to show the structures of the sesquiterpenes like cedrene, cariophyllene, longifolene, and tricyclovetivene, while over a decade the hydrocarbon $C_{15}H_{24}$ has not yielded to study by classical methods based on dehydrogenations and oxidations [9].

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Received July 22, 1957

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Concerning the [illegible]

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.